Pediatrics

VOLUME 1 APRIL 1948 NUMBER 4

ORIGINAL ARTICLES

ENCEPHALOPATHIES FOLLOWING PROPHYLACTIC PERTUSSIS VACCINE

By RANDOLPH K. BYERS, M.D., AND FREDERIC C. MOLL, M.D.
Boston, Mass.

INTRODUCTION

INFLAMMATORY reactions involving various parts of the nervous system following injections of various sera or vaccines have long been known but, so far as we are aware, no one has described the severe encephalopathies which have been observed following the prophylactic use of pertussis vaccine in infants. Madsen[1] in his report on the prophylactic inoculations of 1,832 Faroe Islanders mentioned the death of two small infants in convulsions beginning one or two hours after injections of fluid pertussis vaccine. He reported that autopsies failed to disclose any adequate cause of death. Werne and Garrow[2] reported the death in shock of a pair of identical twins 16 and 24 hours respectively after the second injection of alum-precipitated diphtheria toxoid and pertussis antigen. Careful post mortem examination showed widespread vascular injury. Convulsions, said to be ephemeral in character, have been reported by a number of observers. Doull, Shibley, and McClelland[3] reported three children with convulsions among 496 children immunized with fluid vaccine. Taylor[4] reported a reaction to the vaccine of a ten-month-old boy characterized by subnormal temperature, limpness, and convulsions coming on a few hours after the injection. Recovery was stated to be complete in a few hours. Kendrick and Eldering[5] reported the immunization of 1,815 children, 6 to 15 months of age, by 9,075 injections, with one reaction characterized by convulsions. Sako[6] and his co-workers reported two instances of convulsions following

From the Department of Pediatrics, Harvard Medical School and from the Infants' and Children's Hospitals, Boston, Mass.

Read at the meeting of the American Pediatric Society, Stockbridge, Mass., May 13, 1947.

The work reported in this paper was supported in part by the Bay State Society for the Crippled and Handicapped.

For comment see Editorial, page 579.

(Received for publication October 27, 1947.)

6,600 injections of H. pertussis alum-precipitated vaccine, and in a personal communication Sako states that in approximately 105,000 children immunized to pertussis, there have been four transient convulsions. Many large series, such as the early ones of Sauer[7] involving 3,974 children and the later one of Cravitz and Cauley[8] including 5,000 children, have been reported without reference to such accidents.

It has been accepted for years that virus vaccines, such as those of vaccinia and rabies, occasionally produce encephalopathies and myelopathies (Turnbull[9] and Bassoe[10]). The question of the occurrence of such lesions following revaccination remains obscure, since the available evidence in the literature (Comby[11] and Guerido[12]) is inconclusive. That sera and bacterial vaccines can produce similar changes has been shown by Ayer[13] for the peripheral nerves (antitetanic serum), by Kennedy[14] for peripheral nerves, cord, and brain (typhoid vaccine), and by Winkleman and Gotten[15] for various parts of the nervous system following both sera and vaccines. Curphey[16] has recently reported the death in convulsions of a three and one-half year old girl after inoculation with Influenza A and B vaccine. Autopsy showed widespread pathologic lesions, principally vascular. A reaction involving antigen and antibody has been suspected by many as a possible explanation of such disease processes, and Ferraro[17] recently has reviewed the literature on this point extensively and has added observations of his own.

That a specific toxin might be responsible for the cases reported remains another possibility, and such a product of H. pertussis was suspected by Bordet and Gengou[18] in their original description of the organism. Their observations were first amplified by Tessier[19] and his co-workers, and subsequently many workers[20–27] have described toxins produced in a variety of ways from cultures of the bacillus. All observers agreed that a toxin, or toxins, were produced by appropriate cultures, but that such products were very unstable and difficult to prepare and preserve. Since most of the above observers were interested in the antigenic properties of the toxins, autopsy studies of their effects were mentioned only incidentally. They proved fatal to mice and guinea pigs and necrotizing to the skins of rabbits. After either intravenous or intraperitoneal injection, lesions of the organs of the peritoneal cavity were the most common findings in fatal experiments.

Fonteyne and Dagnelie[28] prepared an endotoxin which produced a diffuse encephalitis and death when injected into either the cerebral substance or subarachnoid space of rabbits or guinea pigs. Various control substances produced from other organisms, or the heated pertussis endotoxin used in the same way, did not reproduce the results. Nakamura[29,30] produced encephalitic changes in rabbits with a combination of agents, among them intravenous injections of cultures of H. pertussis. He also produced both an endotoxin and an exotoxin from the same cultures which, when injected into the subarachnoid spaces of rabbits, caused a rapidly fatal encephalitis.

Clinical Observations

During the past few years, several children were admitted to the Children's Hospital in Boston in convulsions beginning a few hours after the injection of prophylactic pertussis vaccine. Their stories were so similar that during the past winter we have made a search through the records of the hospital for the past ten years, and have found 15 similar instances, which form the basis of the present report.

Twelve of the children were boys and three were girls, a sex difference also encountered in relation to other substances, such as lead, causing gross injury to the

developing nervous system.[31] At inoculation time, the children varied in age between 5 and 18 months. Developmental data were obtained in detail on all but two of the children, whose mothers simply stated that they had developed normally. Reference to the case histories showed that such objective activities as sitting, walking, and talking had appeared in many of the children prior to the inoculations; and that regressions or

TABLE I

ETIOLOGIC FACTORS

Case	Age at Time of Injection	Sex	Injection Causing Reaction	Dose in Billions of Organisms	Time Interval to Onset of Symptoms	Severity of Symptoms	Residence
1	15 months	Male	3rd	?	18 hours	Severe	Fall River, Mass.
2	10 months	Male	2nd	30	1 hour	Severe	Boston, Mass.
3	12 months	Male	2nd	40	4 hours	Severe	Boston, Mass.
4	7 months	Female	3rd 4th	40 12	4 hours 12 hours	Severe Severe	Hartford, Conn.
5	18 months	Male	1st	40	20 minutes	Moderate	Boston, Mass.
6	8 months	Male	1st 2nd	20 30	8 hours 72 hours	Mild Severe	Arlington, Mass.
7	11 months	Male	3rd	40	8 hours	Severe	Medford, Mass.
8	10 months	Male	1st	20	6 hours	Severe	Boston, Mass.
9	6 months	Male	3rd	45	11 hours	Severe	Newton, Mass.
10	9 months	Male	1st	20	20 minutes	Severe	Fall River, Mass.
11	5 months	Female	1st	?	6 hours	Severe	Fisher's Island, Conn.
12	7 months	Male	3rd	40	24 hours	Severe	Boston, Mass.
13	6 months	Male	2nd	40	24 hours	Severe	Salem, Mass.
14	6 months	Male	1st 2nd	10 10	12 hours 12 hours	Severe Severe	Quincy, Mass.
15	7 months	Female	3rd	10	10 hours	Severe	Putnam, Conn.

failure of further development occurred after the encephalopathies in several instances. In so far as it was possible to judge none of the children were defective prior to their acute illness. None had had convulsions.

Family histories were of interest in respect to three patients. In Case 2, two out of three siblings had epilepsy, apparently idiopathic, and an uncle was hydrocephalic. One of two siblings of Case 9 was hydrocephalic and, finally, a younger sibling of Case 12 had "febrile convulsions" five years after the onset of the patient's illness.

The injections were given between 1939 and 1947. There was no concentration in any one year. No cases originated in 1940 and 1942, and the number of cases in each of the other years varied from one to four. Geographically, the patients came, as would be expected, from Greater Boston in nine instances, two were from Fall River, Mass., and one each from Hartford, Conn., Fisher's Island, Conn., Putnam, Conn., and Salem, Mass.

The only common precipitating agent was some form of pertussis vaccine. In 12 instances fluid pertussis vaccine was used, in two cases combined diphtheria toxoid (in one instance fluid and in the other alum-precipitated) and fluid pertussis vaccine was used, in one case the triple antigen of diphtheria and tetanus alum-precipitated toxoid and fluid pertussis vaccine was used, and in one case the triple antigen, all of whose components had been treated with alum, was used. The usual dosage schedule of three doses, respectively, 20 billion, 40 billion, and 40 billion bacteria or less was used in all instances save one, in which an initial dose of 40 billion bacteria was followed in a matter of minutes by irritability, coma, fever, and convulsions. In two instances the size of the dose was not recorded. Six children reacted explosively to the first dose, three to the second dose, and six to the third dose. In addition, three children, who had had convulsive reactions to an earlier dose, reacted again with convulsions following a succeeding dose.

The products of eight different manufacturers were identified by the doctors who gave the inoculations as having been used. Although one manufacturer was represented five times and another three times, these two between them supply a large proportion of the biologicals used in and about Boston.

The explosive reactions began as soon as 20 minutes and as long as 72 hours after the inoculations. The outstanding symptom among the group was convulsions, which varied from a few minutes to several days in duration. Changes in consciousness, varying from drowsiness or irritability to deep coma, occurred in all. It is noteworthy that milder reactions had occurred following an earlier dose of vaccine in two instances; one patient was irritable and had a blotchy rash and a second was feverish and lethargic for two days.

Six of the patients were admitted to the hospital at the time of the acute episodes. All showed various neurologic signs associated with cerebral disease, five were described as comatose, four had hemiplegia, and two had generalized hyperreflexia with bilateral clonus and Babinski signs. In none were the ocular fundi abnormal.

Spinal fluid examinations on these six children were normal in one; i.e. no cells and total protein 29 mg./100 cc. fluid. In the remainder the total protein varied from 35 mg./100 cc. to 86 mg./100 cc., and the cell counts from 0 to 35 mononuclear cells per cmm. Two spinal fluids were examined in other hospitals at the time of the acute attacks: one was reported as normal and the other showed a negative Pandy test and 63 monocytes per cmm. White blood cell counts on the acutely ill patients varied from 10,000 to 20,000 per cmm., and the predominant cells were polynuclear neutrophiles in proportions from 58% to 86%.

In the whole series, the acute illness varied in length from 36 hours to 10 days. After this, one child had three convulsions scattered over a five month period, but in the two year follow-up period had remained well and development seemed satisfactory to his mother. The remaining 14 children suffered from a variety of continuing difficulties, because of which nine were brought to the hospital for the first time. It is obvious that

this method of selections of patients probably weighted the series with individuals who did badly.

Intellectually, 4 infants between 11 and 26 months of age appeared intact 4 to 14 months after their acute illness. One child, seen only once, one month after discharge from the hospital, had not yet regained his speech, which had been present before the inoculations. A sixth infant, who had recurrent convulsions for two months after his encephalopathy, had a complete remission of convulsions for four months following pneumoencephalography. Although he still showed a mild right hemiplegia, his mother felt that his development, while slower than that of his older siblings, was accelerating.

TABLE II

FINAL STATUS

Case	Follow-Up Age in Months	Time in Months Since Vaccine	Examination		EEG	PEG
			Neuro.	Mental		
1	32	17	C.P. *	+	Normal	Not done
2	19	9	C.P. *	±	Normal	Enlarged ventricles
3	31	19	*	+	Normal	Not done
4	48	38	*	−	3 sec. Wave & spike	Enlarged ventricles
5	19	1	C.P.	+	Not done	Not done
6	20	12	C.P. Blind	−	3–5 sec. Slowed	Enlarged ventricles
7	14	3	C.P. * *	+	Slow wave. Focus left	R. vent. >l. ? normal
8	30	20	Died of pneumonia *	−		
9	12	6	Died of pneumonia		Not done	Enlarged ventricles. r. >l.
10	76	66	*	−	Slow & fast	Enlarged ventricles
11	32	27	C.P. Blind	−	2 sec. Wave & spike	Enlarged ventricles
12	8 yrs.	90	*	−	Spike focus. Left temporal	Enlarged r. lateral ventricle
13	34	28	Normal	+	Normal	Not done
14	17	11	*	−	3–5 sec. Slowed	Enlarged ventricle
15	11	4	*	+	2½–4 sec. Slowed	Normal

C.P. Cerebral palsy.
* Recurrent convulsions.
+ Normal mentality.
− Retarded mentality.

A seventh patient had a four month period following his acute episode, during which he appeared to be developing normally, only to go into status epilepticus when 14 months of age, at the onset of an upper respiratory infection. From this time on he pursued a steadily deteriorating course, ending in death in an institution. The remaining eight patients showed more or less severe retardation. In several instances, such as Cases 3, 7, and 8, development had progressed far enough prior to the inoculation to allow a clear statement of intellectual regression after the acute episode. Four children, who had inoculations four years or more ago, were given psychologic examinations by Dr. Edith Meyer during the past winter. All showed defects of attention, irregularities of mental development most marked in relation to abstract behavior, and difficulty in organizing material; in short the sort of psychologic variations found by a number of writers[32–34] to result from diffuse postnatal brain injury. Three children were grossly defective, of whom one (in addition to the child mentioned above) died, also in an institution.

Recurrent convulsions, either grand mal, petit mal, or localized in type, continued over variable lengths of time in 13 children. In three of these, remissions varying in length from three months to two years have occurred, but in the remaining ten the convulsions have continued either to the death of the patient or to the present time.

Seven of the living children, at the time of the last contact, showed other evidences of cerebral damage: five had hemiplegias and two were virtually decerebrate. Among these, Cases 1, 3, 5, and 7 were walking without evidence of cerebral palsy prior to their inoculations.

In summary, therefore, one child had recovered completely, three had had too short a period of observation to allow for final conclusions, two pursued a long down-hill course ending in death, and the remaining nine suffered from damage to their nervous system, which in most instances promised to interfere with competitive living.

Of eight pneumoencephalograms done during the follow-up period, six showed dilatation of the ventricular system and two were at the upper limit of normal. Of ten electroencephalograms, six were normal and the remaining four were abnormal.

TABLE III

ENCEPHALOPATHY DURING PERTUSSIS—26 CASES
7 MONTHS AND UNDER—13 CASES

Outcome	
Satisfactory to family	6
Mental retardation	6
Chronic convulsions	3
Cerebral palsy	1
Dead	7
Unknown	3

To control the possibility that coincidence played an important part in the production of these encephalopathies following pertussis vaccine, the hospital records were consulted as to the incidence of vaccinial encephalitis. Since Massachusetts has a law requiring all children be vaccinated prior to school admission, it seemed certain that a greater proportion of the population were exposed to this vaccine than to pertussis vaccine. That vaccination is a cause of encephalomyelitis is well established (Bijl[35] and Finley[36]). During the same ten years there were admitted to the Children's Hospital eight cases of this latter condition. Either the encephalopathy following pertussis vaccine must be more common, under present conditions of usage, or more severe or more devastating than that following vaccination against smallpox, since it seems doubtful if more than one-quarter of the children in Massachusetts receive pertussis vaccine. It should be noted that pertussis vaccine is used largely in infancy and smallpox vaccine, by and large, is used in this state as children approach school age. The literature would lead one to suspect that smallpox vaccination was accompanied by a greater risk at five years than in infancy, while the reverse may be true of pertussis vaccine. Though some of the children with encephalopathy following pertussis vaccine came from states other than Massachusetts, vaccination customs are virtually the same in them.

During this same ten year period, there were also admitted to the Children's Hospital 26 children suffering from the acute or chronic effects of encephalopathy accompanying

pertussis itself. Of these, 13, or one-half, were seven-months-old or younger and would not have had time since birth to be immunized according to the usual practice at present in vogue. Of these small infants, one had had a single dose of hyperimmune serum during the incubation period; otherwise no prophylactic treatment had been attempted. Among the 13 older children, one had had a course of pertussis vaccine ending approximately six weeks prior to the onset of her pertussis, and another had received two doses of pertussis vaccine as treatment for her disease. Her encephalopathy began explosively 18 hours after the vaccine, and might just as well be charged to the vaccine as to the pertussis.

Of the entire group of 26 children with encephalopathy following pertussis, six were satisfactory to their families six months to ten years after their acute illness, seven died of their acute illness, three could not be found, and the remaining ten were sufficiently damaged to make competitive living unlikely. Good and bad outcomes seemed for this small group to be impartially distributed between the younger and older children.

Summary

Inspection of the records of the Children's Hospital for the past ten years has disclosed 15 instances in which children developed acute cerebral symptoms within a period of hours after the administration of pertussis vaccine. The children varied between 5 and 18 months in age and, in so far as it is possible to judge children of this age range, were developing normally according to histories supplied by their parents. None had had convulsions previously. Many different lots of vaccine, made by eight different manufacturers over a period of eight years, were implicated. The inoculations were given throughout the usual geographic range of children coming to this hospital. All but one, at the time of follow-up or death, showed evidence of impairment of the nervous system, which might still have been in the healing stage in three or four.

During the same period about half as many children were seen in the hospital suffering from the encephalopathy secondary to smallpox vaccination, and about twice as many from the encephalopathy complicating pertussis itself.

A variety of etiologic considerations were suggested by consideration of the reported cases and references to the literature. That constitutional factors may have been involved was suggested by both the preponderance of males as opposed to females, and by the high incidence of abnormalities of the nervous system in the family histories. The clinical course and cytologic abnormalities of spinal fluids found in acute cases indicated an encephalopathy. The literature suggested that this process might have resulted from either the activity of a specific toxin or from an antigen-antibody response. Against the former of these hypotheses was the unstable nature of the heretofore recognized toxins which could hardly survive in properly aged vaccines. The rapid onset of symptoms, occasionally within minutes of the first injection, seemed strong evidence against the second. The present study has left these etiologic considerations unanswered, but it has called attention to a risk of the prophylactic use of pertussis vaccine not hitherto recognized.

In view of the impressive evidence of the effectiveness of prophylactic pertussis vaccine now accumulating, it seems likely that babies are safer vaccinated than not. Further studies should be made to prove this point definitely, for the encephalopathy following pertussis vaccine seems more devastating than the vast majority of the nervous lesions following the use of smallpox vaccine.

Conclusion

In common with many other biologic materials used parenterally, an important risk of encephalopathy attends the use of prophylactic pertussis vaccine. The mechanism whereby the encephalopathy is produced is not elucidated by the present study. The universal use of such vaccine is warranted only if it can be shown to be effective in preventing encephalopathy or death from pertussis itself in large groups of children. If avoidance of the inconvenience of the average attack of pertussis is all that is expected, the risk seems considerable. Efforts to diminish the hazard by modification of the vaccine or new methods of administration seem indicated.

Case Histories

#1, D.H. (Seen through the kindness of Dr. Bronson Crothers). Male—21 months. Entered because of left hemiparesis. Family History: F., M., and two siblings living and well. Past History: Normal, walking, talking. Present Illness: At about 14 months given first two inoculations of combined diphtheria toxoid (alum-precipitated) and pertussis vaccine. At 15 months, in April 1945, in Fall River, Mass., given third inoculation of diphtheria toxoid (alum-precipitated) and pertussis vaccine (amount and manufacturer unknown). Eighteen hours later developed a fever of 40.5° C. and had a severe left-sided convulsion, which was controlled finally with sodium phenobarbital. Following the convulsion, was unresponsive and had a spastic left hemiplegia. Admitted to another hospital, where he continued to have left-sided convulsions. These gradually diminished, and the left hemiparesis improved. Laboratory findings: WBC 20,000/cmm. with 58% polynuclear leucocytes and normal spinal fluid. Discharged very much improved, but with a persistent left hemiparesis. Course: Seen at the Children's Hospital at 21 months. Had had four convulsions in the interval, but otherwise had shown gradual improvement. Examination at that time showed an intellectually able child with a left hemipareis. EEG was normal, showing 6-8 per second waves, with scattered 4's and 5's and no focus. PEG was not done. At 24 months parents wrote that he continued to improve and had no more seizures.

#2, J.R. Male—18 months. Entered because of recurrent convulsions. Family History: F. and M. living and well. Three siblings, of whom two have epilepsy. Past History: Normal, walking. Present Illness: At ten months, in July 1946, in Boston, was given first inoculation of pertussis vaccine (amount and manufacturer unknown) without reaction. Several weeks later received second immunizing dose of 1.5 cc. pertussis vaccine (30 billion organisms—manufacturer "A"). One hour later developed fever and had a severe generalized convulsion. This was followed by stupor, which gradually cleared in three days. Since that time had had recurrent right sided convulsions. Course: At 18 months was admitted to the Children's Hospital. At that time was found to have a moderate right hemiparesis. Psychologic examination revealed a relatively efficient and competent individual. Laboratory findings: WBC 9,200/cmm. negative blood Hinton, and normal spinal fluid with total protein of 13.8 mg./100 cc. fluid. EEG showed 3-5 per second waves with a little 6 per second activity, and was considered normal. PEG (Fig. 1.) revealed considerable symmetrical dilatation of entire ventricular system, basal cisterns, and filled subarachnoid passages compatible with diffuse deficiency of cerebral and cerebellar tissues. Continued to have right-sided convulsions but was improved with phenobarbital. Developmental rate did not seem impaird by his illness.

#3, B.L. Male—25 months. Entered because of convulsive seizures. Family History: F., M., and one sibling living and well. Past History: Normal, walking. Present Illness: At 11 months received 1 cc. pertussis vaccine (manufacturer "B") without reaction. At 12 months, in December 1945, in Boston, received second inoculation of 2 cc. pertussis vaccine (40 billion organisms—manufacturer "B"). Four hours later had a severe generalized convulsion, followed by a right-sided hemiparesis. Entered another hospital where a gradual improvement was noticed within ten days. Following this seemed well until 19 months when he developed recurrent petit mal seizures, which became more frequent. Course: At 26 months admitted to Children's Hospital. Examination was essentially normal except that he did not talk and dragged right leg in walking. Mental status was considered probably normal. Laboratory findings: WBC 7,300/cmm. with 55% polynuclear leucocytes, negative blood Hinton, and negative X-rays of the skull. EEG was considered normal, and showed 4-7 per second waves without focus or seizure discharges. PEG was not done. Attacks had

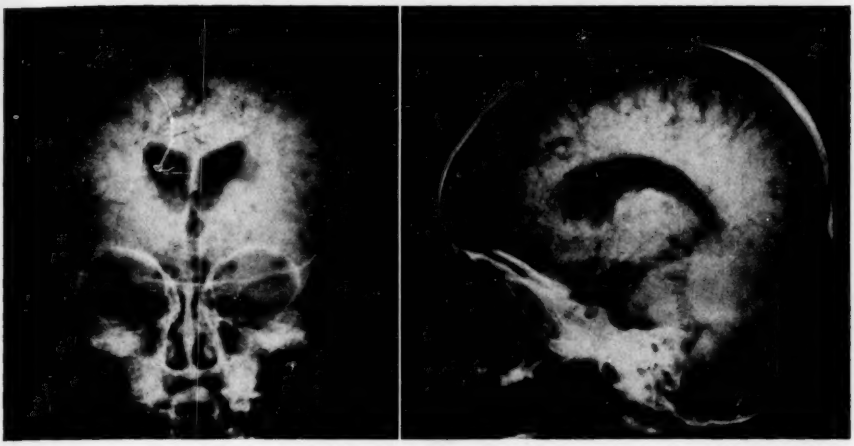


FIG. 1. Pneumoencephalogram in Case 2 seven months after inoculation, showing slight dilatation of lateral and third ventricles.

not been controlled by various drugs. At 31 months intellectual status had not advanced beyond that found at 26 months, and was definitely retarded and irregular. Had not developed speech, and was having many attacks weekly, which were uncontrolled by a variety of drugs. Physical examination showed a very obvious right hemiplegia with contractures of the heel cord. An electroencephalogram (Fig. 2.) showed a few scattered spikes and a good many slow waves, at the rate of 3-4 per second, most marked in right occipital lead.

#4, J.P. Female—10 months. Entered because of recurrent convulsions. Family History: F. and M. living and well. No siblings. Past History: Normal, sat alone at seven months. Present Illness: At about seven months was started on a course of immunization for pertussis, and had first and second inoculations without incident (manufacturer "C"—amount unknown). At seven and one-half months, in September 1943, in Hartford, Conn., was given third pertussis inoculation of 2 cc. pertussis vaccine (40 billion organisms—manufacturer "C"). Six hours later developed a high

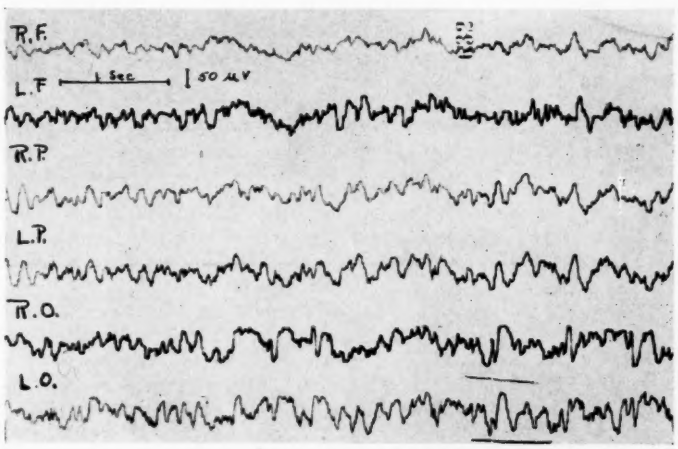


FIG. 2. Electroencephalogram in Case 3 showing spike in occipital leads, 19 months after inoculation.

fever and had a severe generalized convulsion. In the next few days had three or four more generalized convulsions, which were treated symptomatically, and recovered promptly without sequelae. Three weeks after the third pertussis inoculation, a fourth was given, of 0.3 cc. pertussis vaccine, doubly concentrated, precipitated (about 12 billion organisms—manufacturer "D"). Twenty-four hours later again had a severe generalized convulsion. Again recovered promptly, but since that

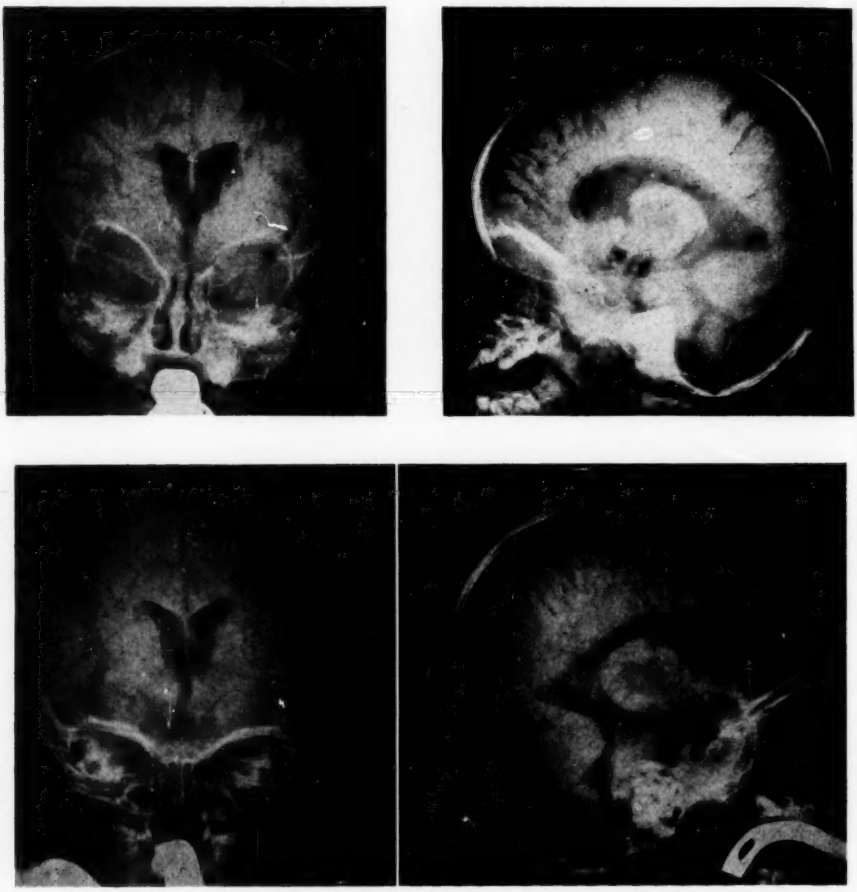


FIG. 3. Pneumoencephalograms in Case 4 two months and twelve months after last inoculation of pertussis vaccine, the second series showing some restitution of brain mass, though the lateral and third ventricles are still mildly dilated.

time development seemed to be retarded. Course: At 10 months admitted to the Children's Hospital. At that time appeared well but somewhat retarded for age, in that she did not sit up or pull up. Laboratory studies: Normal urine, WBC 6,150/cmm. with 64% polynuclear leucocytes, and a clear spinal fluid with total protein of 9.5 mg./100 cc. fluid. Subdural taps were negative. EEG showed abnormally slow activity with several three per second waves and spike discharges and amplitude asymmetry, with higher voltage on left. PEG (Fig. 3.) revealed moderate dilatation of lateral ventricles, third ventricle, and aqueduct. Basal cisterns and subarachnoid pathways were also dilated. The appearance was considered campatible with a moderate and diffuse deficiency of

cerebral tissues. Following discharge development progressed satisfactorily, but she had numerous petit mal and occasional grand mal seizures. Was readmitted to Children's Hospital at 21 months for reevaluation. At that time she seemed to be a competent child who had developed normally, but who had numerous petit mal seizures. Repeat EEG (Fig. 4.) showed 3 to 7 per second waves in all leads, with occasional bursts of petit mal wave and spike. PEG (Fig. 3.) revealed slight persistent symmetrical dilatation of the entire ventricular system and basal cisterns. She was discharged on trimethadione (tridione) and has continued to improve, with gradual lessening of the petit mal, although her mother considers her development still somewhat retarded. Letter from mother at four years states condition is about the same.

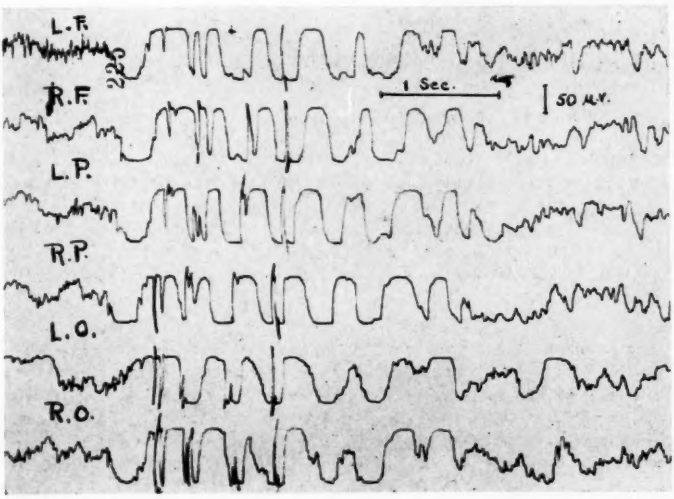


FIG. 4. Electroencephalogram in Case 4 showing wave and spike complexes three years after last inoculation of pertussis vaccine.

#5, J.M. Male—18 months. Entered because of coma of 24 hours' duration. Family History: F. and M. living and well. One sibling in third week of whooping cough. Past History: Normal, walking. Present Illness: Because of family exposure to pertussis was given at 18 months, in May 1945, in Boston, first inoculation of 2 cc. pertussis vaccine (40 billion organisms—manufacturer "E"). About 10 to 20 minutes later became drowsy, then unresponsive, rigid, and febrile. Because of continuing intermittent generalized convulsions, was admitted to Children's Hospital 24 hours later. Course: Examination showed a well developed child in semicomatose state, responding only to painful stimuli. Deep reflexes were exaggerated, and bilateral Babinskis, Oppenheims, and ankle clonus were obtained. Laboratory findings: Normal urine, WBC 10,000/cmm. with 64% polynuclear leucocytes, negative blood Hinton, and negative 1-1000 tuberculin skin test. Throat cultures for pertussis were negative and spinal fluid was normal except for a total protein of 49.5 mg./100 cc. fluid. Was treated symptomatically and improved rapidly, although he never spoke while in the hospital. When seen at 19 months had a slight right hemiparesis, brought out on walking. Was learning a few words and seemed fairly competent. PEG and EEG not done.

#6, R.M. Male—8 months. Entered because of convulsions of three weeks' duration. Family History: F., M., and one sibling living and well. Past History: Normal, held head up at five months and was rolling over at seven months. Present Illness: At seven months was given first inoculation of 1 cc. pertussis vaccine (20 billion organisms—manufacturer "E"). Following this developed irritability and drowsiness, which cleared in about three days. Three weeks later, in December 1944,

in Arlington, Mass., was given second inoculation of pertussis vaccine, 1.5 cc. (30 billion organisms—manufacturer "E"). Rapidly became irritable, restless, febrile, and held right arm stiffly. About 72 hours after the inoculation had two severe generalized convulsions and was admitted to another hospital. On admission was febrile and was having generalized convulsive seizures. Lumbar puncture revealed clear spinal fluid with a total protein of 26 mg./100 cc. fluid. WBC was 10,000. Had repeated convulsions and improved very slowly. X-rays of the long bones, subdural taps, and repeated lumbar taps were done, but none was contributory. Nineteen days after onset was admitted to Children's Hospital. Course: On admission, at eight months was semi-comatose, febrile, and rigid, more marked on the right. Initial laboratory studies: Leucocytosis of 20,000, normal spinal fluid, and negative blood Hinton and tuberculin skin test. Had intermittent convulsive seizures controlled with phenobarbital. EEG showed 3 to 5 per second waves without seizure discharges, which was considered normal for age. PEG (Fig. 5.) revealed marked symmetrical dilatation of each lateral ventricle. Third and fourth ventricles were adequately visualized, but the basal cistern appeared dilated and some subdural air was present. Showed little improvement during hospitalization. When seen by his family physician 8 months after discharge, at 16 months, he was blind, deaf, spastic, and helpless.

#7, P.Q. Male—11 months. Entered because of convulsions. Family History: F., M., and two siblings living and well. Past History: Normal, sat alone at 7 months and walked at 11 months. Present Illness: At nine months received first inoculation of combined diphtheria toxoid and pertussis vaccine. The second dose was given at ten months of age, following which he had fever for several days. At 11 months, in December 1946, in Medford, Mass., received third dose of fluid diphtheria toxoid and fluid pertussis vaccine (40 billion organisms—manufacturer "E"). Eight hours later had a severe right-sided convulsion controlled only with sedation. Because of the convulsion, was admitted to Children's Hospital. Course: On admission was febrile and was having a right-sided convulsion. Examination was otherwise negative. WBC was 13,000 with 71% polynuclear leucocytes. Spinal fluid had normal sugar, 3 monoclear cells, and a total protein of 51 mg./100 cc. fluid. Cultures were negative. Blood Hinton and tuberculin skin test, 1-1000 and 1-100, were negative. Skull X-ray films were negative. Convulsions were controlled with sedation, and he soon became responsive, but a slight hemiplegia persisted. EEG showed 1 to 3 per second waves with some 4 to 6 per second waves, and the slowing was more marked in the whole left hemisphere in the waking record. The sleep record showed more slowing on left with amplitude asymmetry. This was interpreted as a grossly slowed EEG with slow wave focus in left hemisphere and amplitude asymmetry, with higher voltage on left. At 13 months seemed improved but continued to have right side convulsive seizures and a persistent right hemiplegia. PEG (Fig. 6.) demonstrated that the ventricular system was top normal in size. Left posterior horn appeared considerably larger than right. Basal cisterns were normal in size, except that cisterna pontis appeared enlarged. Subarachnoid, subdural, subtentorial air was visualized. At 16 months he still had mild hemiplegia, was pulling himself to his feet on furniture and drooled constantly. Had had no convulsions in the past four months. His mother felt that he was not learning as rapidly as her two older children at the same age, though obviously improving.

#8, H.G. Male—10 months. Entered because of convulsions. Family History: F., M., and one sibling living and well. Past History: Normal except for spasmus nutans, for which he was seen in the Out-Patient Department. At that time he seemed competent. Present Illness: At ten months, on September 16, 1941, in Boston, was given first inoculation of pertussis vaccine (20 billion organisms—manufacturer "F"). Soon afterward developed fever and irritability. Six hours later had a generalized convulsion and was admitted to Children's Hospital. Course: On admission was febrile and was having a generalized convulsion. WBC was 10,000 with 86% polynuclear leucocytes. Urine, blood Hinton, skull X-ray films, and tuberculin skin test, 1-1000, were negative. Spinal fluid was negative except for the total protein of 70 mg./100 cc. fluid. In the hospital he soon became afebrile and convalesced rapidly, and at 14 months was walking and beginning to say a few words. Remained well until 14 months when he again had a severe generalized convulsion. Was readmitted to Children's Hospital. Examination revealed a febrile child having generalized convulsions. There was a mild upper respiratory infection. Laboratory findings at that time: Leucocytosis of 26,000 with 55% polynuclear leucocytes, and clear spinal fluid with a total protein of 15 mg./100 cc. fluid. Blood

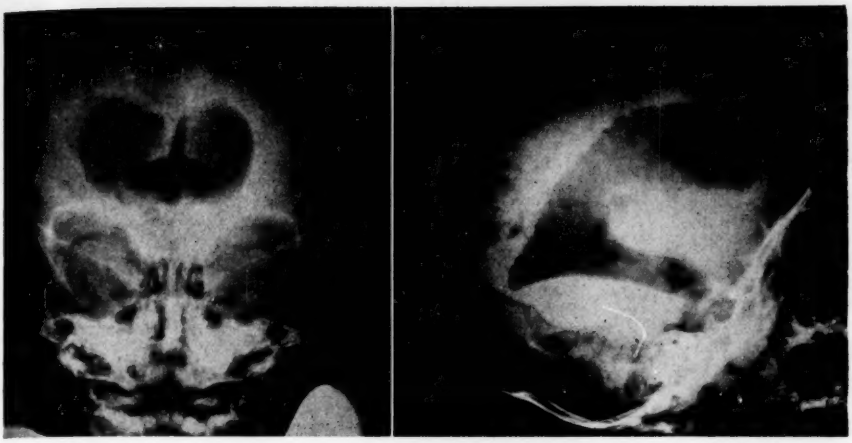
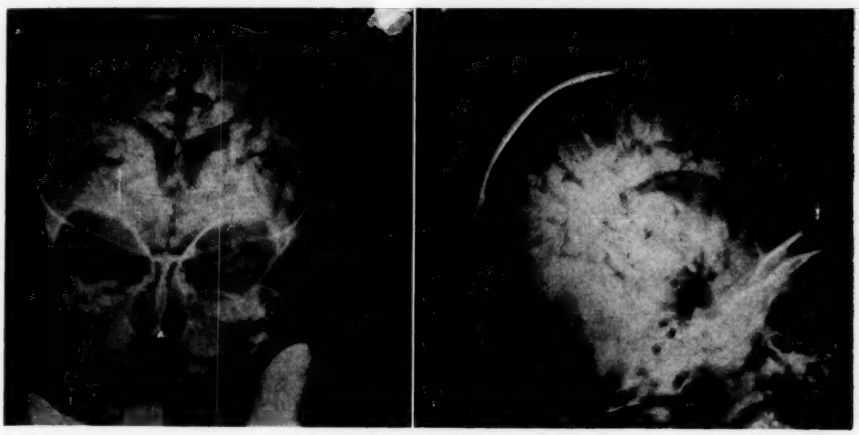


FIG. 5. Pneumoencephalogram in Case 6 one month after last inoculation of pertussis vaccine, showing enormous dilatation of the ventricular system.



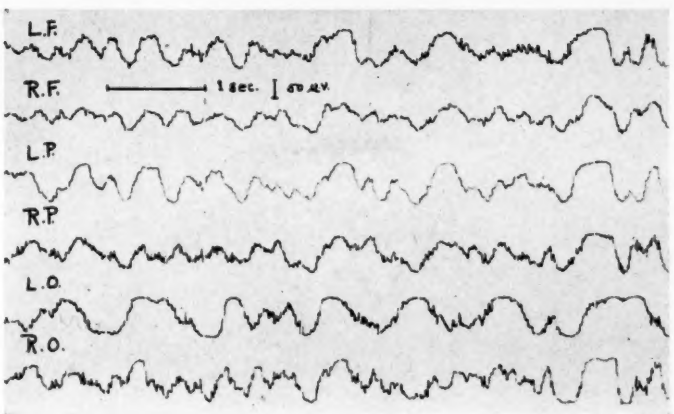


FIG. 6. Pneumoencephalogram and electroencephalogram in Case 7 two months after pertussis vaccine and diphtheria toxoid. Slight asymmetry of lateral ventricles, left being larger, and left slow wave focus involving entire hemisphere respectively.

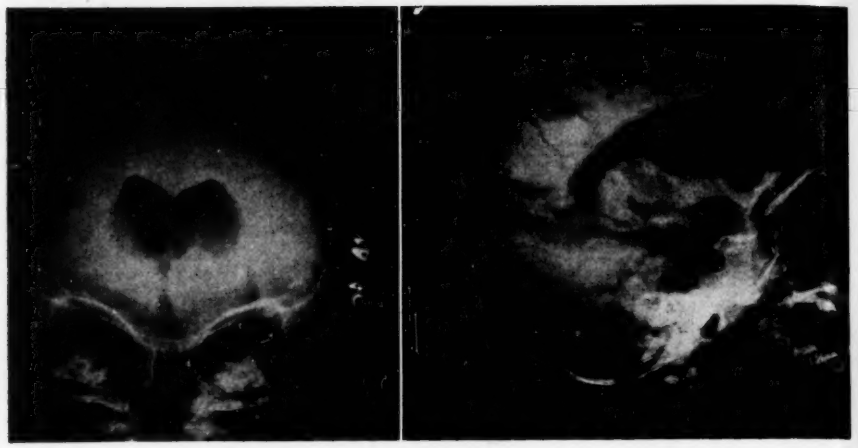
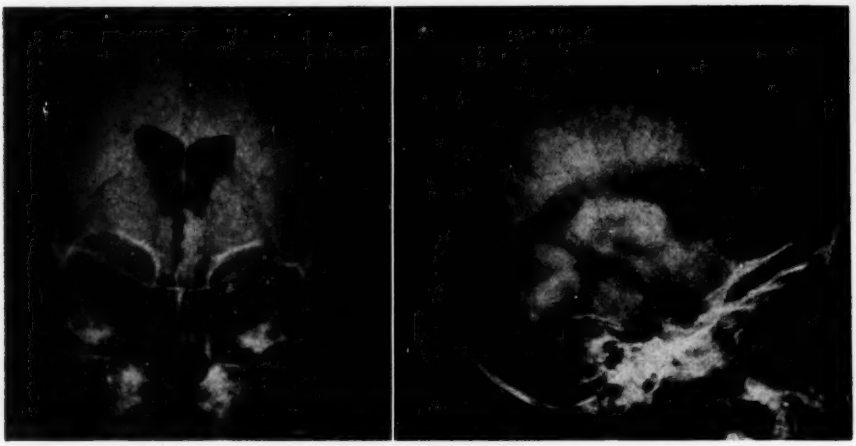


FIG. 7. Pneumoencephalogram in Case 9 one month after last dose of pertussis vaccine, showing moderate dilatation of lateral and third ventricles.



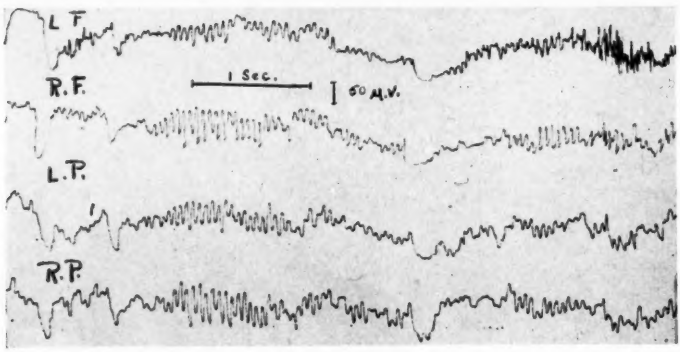


FIG. 8. Pneumoencephalogram and electroencephalogram in Case 10 three and one-half years after last dose of pertussis vaccine, showing moderate dilatation of the ventricular system and bursts of rather high voltage fast activity respectively.

culture showed pneumococcus, type XIV, in one flask. Convulsions persisted and were controlled with difficulty. The infection was controlled with sulfadiazine. Bilateral otitis media developed. Myringotomies were performed with the release of pus. However, the patient deteriorated rapidly, both psychologically and neurologically. In search of a cause for the deterioration, bilateral antrotomies were done, which were negative. PEG showed considerable air in subdural spaces and dilatation of both lateral ventricles, most marked on the left. Many subarachnoid pathways were also dilated. He did not improve and, at 16 months was transferred to a state institution where he pursued a down-hill course ending in death at two and one-half years. Autopsy done then showed diffuse atrophy and gliosis of brain with terminal pneumonia.

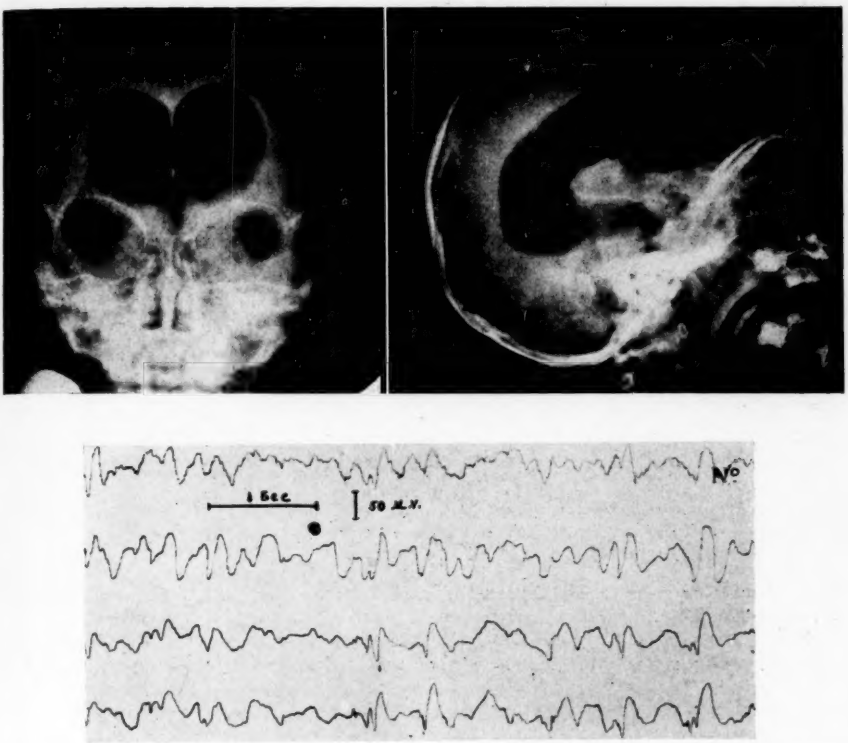


FIG. 9. Pneumoencephalogram and electroencephalogram in Case 11 two years after last inoculation of pertussis vaccine. Patient had had many acute infections and acute glomerulonephritis accompanied by convulsions in the interval. Enormous dilatation of lateral and third ventricles and many spikes in all leads.

#9, R.M. Male—6 months. Entered because of convulsions. Family History: F., M., and one sibling living and well. Another sibling had hydrocephalus and was institutionalized. Past History: Normal, held his head up at two months and sat with support at six months. Present Illness: At four and one-half months received first inoculation of 1 cc. pertussis vaccine (15 billion organisms—manufacturer "F"). The second dose of 2 cc. pertussis vaccine (30 billion organisms—manufacturer "F") was given at five months, followed by generalized maculopapular rash. The rash cleared in three days without sequelae. Third dose was given on September 22, 1941, in Newton, Mass., at six months, of 3 cc. pertussis vaccine (45 billion organisms—manufacturer "F") and was followed by fever, irritability, and 11 hours later by a generalized convulsion. The

convulsion soon recurred and on this account was admitted to Children's Hospital. Course: On admission was stuporous and the odor of paraldehyde was apparent on his breath. Reflexes were hyperactive, and bilateral Babinskis and ankle clonus were obtained. Laboratory findings: Negative urine, blood Hinton, and tuberculin skin test 1-1000. Spinal fluid was clear with a total protein of 29 mg./100 cc. fluid. WBC was 17,000 with 67% polynuclear leucocytes. He improved rapidly and was discharged only to be readmitted four days later because of recurrent convulsions. Examination and laboratory findings were essentially the same as on previous admission. Convulsions persisted throughout the hospital stay. PEG (Fig. 7.) showed moderate dilatation of ventricular system without any filling defect. The left subarachnoid pathways did not fill but those on right were dilated.

FIG. 10-a. Pneumoencephalogram in Case 12 showing localized dilatation of posterior horn of left lateral ventricle, two years after last dose of pertussis vaccine.

There was obvious severe cerebral degeneration, and the patient was discharged to a state institution for care, where he died about six months later of pneumonia. No autopsy was obtained.

#10, S.W. Male—4 2/12 years. Entered because of convulsions. Family History: F., M., and one sibling living and well. Past History: Normal, held his head up at four months and was sitting at eight months. Present Illness: At nine months, in December 1941, in Fall River, Mass., was given first inoculation of 1 cc. pertussis vaccine (10 billion organisms—manufacturer "F"). One hour later developed fever of 40.0° C. and had several generalized convulsions. Following this he had had repeated generalized convulsions, frequently, but not always associated with fever. Because of recurrent convulsions and rather slow development, was admitted to Children's Hospital. Course: Examination at that time revealed immature and irregular adaptive behavior, short interest spans, and general comprehension between two and one-half and three year levels. Laboratory findings; normal urine, WBC 7,500, and clear spinal fluid without increased protein. EEG (Fig. 8.) showed 5-8 per second waves, with frequent bursts of high voltage waves. There were 12-22 per second waves in frontoparietal leads and runs of 3½-4 per second waves in all leads. This was interpreted as a slowing of waves with bursts of abnormally fast activity in frontoparietal leads. PEG (Fig. 8.) showed slight enlargement of both lateral ventricles without filling defect. Third and fourth ventricles were very slightly dilated and basal cisterns and subarachnoid pathways were normal. The patient was discharged unimproved. At six and four-twelfths years of age psychologic examination was still much the same; there had been some increase in language development, but difficulties of attention and deficiencies in relation to special orientation were as marked as ever. He had been unable to learn at all in the first grade and had been excluded from school. Convulsions had occurred at intervals of months.

#11, D.E. Female—2 8/12 years. Entered because of recurrent convulsions. Family History: F., M., and three siblings living and well. Past History: Normal. Present Illness: At five months, in January 1944, at Fisher's Island, Conn., was given one inoculation of pertussis vaccine, (amount and manufacturer unknown). Six hours later developed a generalized convulsion. Since that time had had recurrent convulsions with progressive deterioration of the nervous system. Was hospitalized several times with no improvement. On one admission, at about 2 2/12 years, was said to have had acute glomerulonephritis, but this apparently cleared promptly. Because of severe deterioration and recurrent convulsions was admitted to Children's Hospital. Course: On admission appeared grossly damaged, generally spastic, and utterly helpless. The urine and blood Hinton were nega-

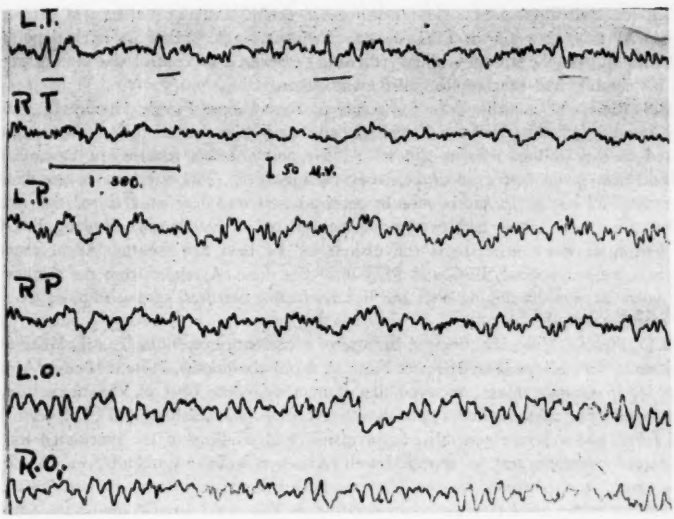


FIG. 10-b. Electroencephalogram showing left temporal spike focus, eight years after vaccine.

tive. WBC 18,100, and there was clear spinal fluid with total protein of 25.5 mg./100 cc. fluid. EEG (Fig. 9) showed 3-5 per second waves with scattered 2 per second, and runs of positive spike discharges in both precentral leads. Slow waves and spikes were also seen in occipitals and both precentral leads. This was interpreted as a seizure record. PEG (Fig. 9.) showed marked dilatation of all ventricles. Basal cisterns were of top normal size, and there were markedly dilated subarachnoid pathways in frontal region. Appearance was that of severe and diffuse deficiency of cerebral tissue. A report from the parents at 3 4/12 years states that she continued to have convulsive seizures and was unable to stand or talk.

#12, S.C. Male—7½ months. Entered because of convulsions. Family History: F., and M., living and well. Two younger siblings, one of whom developed "febrile convulsions" five years after the patient's illness began. Past History: Normal, sat alone at six months and was pulling to his feet at seven months. Present Illness: At about seven months was given first inoculation of pertussis vaccine (20 billion organisms), and one week later second inoculation (40 billion organisms) without reaction. At seven and one-half months, on April 21, 1939, in Boston, was given third inoculation of pertussis vaccine (40 billion organisms—manufacturer "F"). Twelve hours later developed fever and irritability, and 24 hours later had two severe generalized convulsions. Because of the convulsions was admitted to Children's Hospital. Course: On admission he was having a left-sided convulsion. Body temperature was 39.4°C., and a left hemiparesis was found. Urine, blood Hinton, and tuberculin skin test 1-1000 were negative. WBC was 17,300 and spinal fluid was clear with total protein of 34 mg./100 cc. fluid. X-rays of the skull and long bones were negative. The fever subsided by the third hospital day, the hemiparesis improved, and the convulsive state appeared to subside. Readmitted at three years because of intermittent generalized

convulsive seizures and persistent weakness of left arm, leg and left side of face. PEG (Fig. 10-a.) at this time revealed dilatation of right lateral ventricle and rather prominent subarachnoid pathways on the right. EEG showed 3-4 per second waves in precentral and occipital leads. Was discharged home without medication. Seen again at 8 5/12 years of age because of vague abdominal pain. He was attending the first grade with difficulty. A psychologic examination at this time showed a mental age of 7 4/12 years with considerable scatter and an I.Q. of 85-90. Attention spans were short, planning ability poor, and learning ability irregular. Had difficulty in organizing and analyzing form material. EEG (Fig. 10-b.) at this time showed 8-10 per second waves in occipital leads, some 6-8 per second waves, with almost continuous 18-25 per second activity in frontal leads. No seizure discharges. This was interpreted as showing mild slowing with abnormally fast activity. It was thought that the abdominal pain was of psychogenic origin, and the patient was discharged home unimproved. At 8 8/12 years in EEG showed frequent single spikes in left temporal lead and treatment with diphenylhydantoin sodium (dilantin) appeared to control the attacks of abdominal pain, and his conduct had been less impulsive since then.

#13, R.S. Male—11 months. Seen for recurrent convulsions. Family History: F., M., and one sibling living and well. Past History: Essentially normal, but mother thought he was slightly "slow" as compared to the sibling. Present Illness: At five and one-half months, in December 1944, in Salem, Mass., was given first dose of pertussis vaccine 1 cc. (concentration undetermined—manufactured either "E" or "F"). At six months received a second dose of 2 cc. of the same preparation. Twenty-four hours later had two severe generalized convulsions. Following this he seemed well but had three more generalized convulsions in the next five months. At 11 months of age development appeared normal. EEG and PEG were not done. A report from the mother states that at 2 9/12 years he was developing well and had no further seizures, since treatment with phenobarbital had been instituted.

#14, R.D. Male—17 months. Entered because of recurrent convulsions. Family History: F and M. living and well. No siblings. Past History: Normal, sat at six months. Present Illness: At six months, in May 1943, in Quincy, Mass., received first immunizing dose of 1 cc. diphtheria toxoid (alum-precipitated) and pertussis vaccine (10 billion organisms—manufacturer "G"). Twelve hours later developed fever, had a severe generalized convulsion, and swelling of the inoculated leg. The complaints subsided promptly and he appeared well. At seven months a second dose of less than 1 cc. diphtheria toxoid and pertussis vaccine (less than 10 billion organisms—manufacturer "G") was given. Again, 12 hours after this second inoculation he had generalized convulsions. Since that time had had recurrent generalized convulsions of both petit and grand mal type. Course: At 17 months, because of recurrent convulsions, was admitted to Children's Hospital. Physical examination was negative and the laboratory findings showed a negative urine and blood Hinton. WBC 12,500 with 59% polynuclear leucocytes. The spinal fluid was clear with total protein of 9.5 mg./100 cc. fluid. Psychologic evaluation revealed numerous irregularities, with short attention spans and with little learning from experience or imitation. Potential behavior level was seldom reached. EEG showed high voltage 3-5 per second waves in all leads, but no focus, and this was considered definitely slowed for age. PEG showed moderate dilatation of entire ventricular system, basal cisterns, and subarachnoid pathways.

#15, E.B. Female—11 months. Entered because of recurrent convulsions. Family History: F. M., and two siblings living and well. No history of epilepsy or convulsions. Past History: Normal. At four months she rolled over, at seven months sat alone, and at eleven months was pulling herself to her feet in her crib. Present Illness: At six months was given her first dose of 1 cc. "triple vaccine," diphtheria and tetanus alum-precipitated toxoids and alum-precipitated pertussis vaccine (10 billion organisms—manufacturer "H") without reaction. At seven months received a second dose of similar material (manufacturer "A") with some febrile response. At eight months, on April 14, 1947, in Putnam, Conn., received her third dose of 1 cc. of the original material (manufacturer "H"), and was vaccinated against small pox at the same time. About 18 hours later was found in convulsions, which were left sided at times and generalized at times, and continued for six hours intermittently, in spite of 45 mg. sodium phenobarbital intravenously. After the convulsion was stuporous for 12 hours and then showed a flaccid left hemiplegia, which cleared completely in a week. At the time of the convulsion was admitted to another hospital where, because examination disclosed redness of her throat and ears, penicillin and sulfadiazine were administered. A lumbar puncture done on the third day after the injection showed clear spinal fluid with a negative Pandy

test and 63 monocytes per cmm. Cultures and guinea pig inoculations produced no growth. Blood examination the day after the inoculation showed a WBC of 9,200 of which 63% were polynuclear leucocytes, 35% lymphocytes, and 2% monocytes. Urine examination was negative. The smallpox vaccination ran the usual course of a primary reaction, and she was improving rapidly at the time of the take. Three months later developed staring spells, occurring every hour or two, for periods of several days, followed by periods of weeks when no attacks were seen. On two occasions the periods of staring spells were followed by a little diarrhea, and the last of these periods of staring spells was followed by a few days of fever, up to 37.8° C. or 38.3° C. She seemed well for a month, when staring spells developed in connection with an upper respiratory infection and fever. She had these for three days and then developed a convulsion, which began on the left, soon became generalized, and lasted several hours in spite of medication with intravenous sodium phenobarbital. Was brought to the hospital in the convulsion. Course: Physical examination showed a comatose, convulsing child with no evidence of infection. WBC was 30,100 with 85% polynuclear neutrophiles. Spinal fluid examination showed 1 mononuclear cell per cmm. and a total protein of 13.5 mg./100 cc. fluid. Cultures were sterile. The convulsion subsided soon after admission to the hospital, and after a period of stupor she again showed temporary left hemiplegia, no trace of which remained five days later. EEG showed 2½-4 per second waves, with no focus and no seizure discharges. This was considered slightly slowed for age. PEG showed slight inequality of lateral ventricles with slight blunting of right lateral ventricle. There was a good deal of subdural air, considerably greater on the left. PEG was considered normal.

References

1. Madsen, T., Vaccination against whooping cough, J.A.M.A. **101**:187, 1933.
2. Werne, J., and Garrow, I., Fatal anaphylactic shock; occurrence in identical twins following second injection of diphtheria toxoid and pertussis antigen, J.A.M.A. **131**:730, 1946.
3. Doull, J. A., Shibley, G. S., and McClelland, J. E., Active immunization against whooping cough, Am. J. Pub. Health **26**:1097, 1936.
4. Taylor, H. W., Reaction following injection of pertussis vaccine-Sauer, Arch. Pediat. **55**:572, 1938.
5. Kendrick, P., and Eldering, G., Study in active immunization against pertussis, Am. J. Hyg. **29**: 133, 1939.
6. Sako, W., Treuting, W. L., Witt, D. B., and Nichamin, S. J., Early immunization against pertussis with alum-precipitated vaccine, J.A.M.A. **127**:379, 1945.
7. Sauer, L., Present status of preventive inoculations against whooping cough, Am. J. Dis. Child. **54**:979, 1937.
8. Cravitz, L., and Cauley, J. H., Pertussis immunization program of Boston Health Department; comparative value of 2 different antigens, J.A.M.A., **129**:539, 1945.
9. Turnbull, H. M., and McIntosh, J., Encephalomyelitis following vaccination, Brit. J. Exper. Path. **7**:181, 1926.
10. Bassoe, P., and Grinker, R. R., Human rabies and rabies vaccine encephalomyelitis, Arch. Neurol. & Psychiat. **23**:1138, 1930.
11. Comby, Marie Thérèse, Les encéphalites aiguës post-infectieuses de l'enfance, Masson & Cie., Paris, 1935, p. 40, 127.
12. Guerido, A., Encephalitis following revaccination with absence of local reaction and observations on histopathology of post vaccinial encephalitis, Zeitsch. f. d. ges. Neur. & Psy. **125**: 423, 1930.
13. Ayer, J. B., Radiculitis following injections of antitetanic serum, J. Nerv. & Ment. Dis. **81**:676, 1935.
14. Kennedy, F., Certain nervous complications following use of therapeutic and prophylactic sera, Am. J. M. Sc. **177**:555, 1929.
15. Winkleman, N. W., and Gotten, N., Encephalomyelitis following use of serum and vaccine, Am. J. Syph. & Neurol. **19**:414, 1935.
16. Curphey, T. J., Fatal allergic reaction due to influenza vaccine, J.A.M.A. **133**:1062, 1947.
17. Ferraro, A., Pathology of demyelinating diseases as allergic reactions of brain, Arch. Neurol. & Psychiat. **52**:443, 1944.
18. Bordet, J., Gengou, O., L'endotoxine coquelucheuse, Ann. Inst. Pasteur **23**:415, 1909.

19. Tessier, P., Reilly, J., Rivalier, E., and Cambassedes, H., Nouvelles recherches sur l'immunite et la serotherapie anti-endotoxignes; le serum anticoquelucheux, J. de Physiol. et de Path. gen. **27**:549, 1929.
20. Lawson, G. M., Epidemiology of whooping cough, Am. J. Dis. Child. **46**:1454, 1933.
21. Evans, D. G., and Maitland, H. B., Preparation of toxin of H. pertussis; its properties and relation to immunity, J. Path. & Bact. **45**:715, 1937.
22. Evans, D. G., Production of pertussis antitoxin in rabbits and neutralization of pertussis, parapertussis, and bronchosepticus toxins by serum. J. Path. & Bact. **51**:46, 1941.
23. Wood, M. L., Filtrable toxic substances in broth cultures of H. pertussis, J. Immunol. **39**:25, 1940.
24. Strean, L. P., Skin test for susceptibility to pertussis, Canad. M.A.J. **42**:525, 1940.
25. Flosdorf, E. W., Bondi, A., Jr., and Dozois, T. F., Studies with H. pertussis; antigenicity of toxins and relation to other cellular components from several phases, J. Immunol. **42**:133, 1941.
26. Roberts, M. E., and Ospeck, A. G., Pertussis toxin, J. Infec. Dis. **71**:264, 1942.
27. Miller, J. J., Jr., Experimental observations in antigenic potency of H. pertussis extracts, J. Immunol. **26**:247, 1934.
28. Fonteyne, P., and Dagnelie, J., L'action de l'endotoxine coquelucheuse sur les centres nerveux, Comp. Rend. Soc. de biol. **110**:978, 1932.
29. Nakamura, T., Experimentelle Studie über die Keuchhustenmeningoencephalitis, Mitt. a. d. med. Akad. zu Kioto. **28**:596, 1940.
30. *Ibid.* **28**:598, 1940.
31. Byers, R. K., and Lord, E. E., Late effects of lead poisoning on mental development, Am. J. Dis. Child. **66**:471, 1943.
32. Lord, E., and Wood, L., Diagnostic values in visuo-motor test, Am. J. Orthopsychiat. **12**:414, 1942.
33. Strauss, A. A., and Werner, H., Mental organization of brain injured mentally defective child, Am. J. Psy. **97**:1194, 1944.
34. Meyer, E., and Gimmel, M., Psychological appraisal of children with neurological defects, J. Abn. & Soc. Psy. **42**:193, 1947.
35. Bijl, J. P., and Frenkel, H. S., Experimentelle Untersuchungen über Encephalitis post vaccinatoria. Vaccina generalisata beim Kaninchen, Zentralbl. f. Bakteriol. (Abt. 1) **112**:412, 1929.
36. Finley, K. H., Pathogenesis of encephalitis occurring with vaccination, variola and measles, Arch. Neurol. & Psychiat. **39**:1047, 1938.

SPANISH ABSTRACT

Encefalopatias Observadas Despues del Uso Profilactico de la Vacuna Antitosferina

Durante los años de 1939 a 1947 inclusive fueron admitidos en el Hospital de Niños de Boston diez y seis casos que desarrollaron sindrome encefalitico subitamente iniciado dentro de los veiente minutos a setenta y dos horas despues de la inyeccion de vacuna pertussis preventiva.

La edad de los niños inoculados varia entre cuatro y medio y diez y ocho meses. En los niños mayores el desarrollo habia evolucionado lo bastante para presumir adecuada normalidad. Uno habia mostrado "espasmos nutans" antes de la vacunacion, pero habia caminado y pronunciado algunas palabras antes de la inyeccion. Ninguno habia tenido convulsiones antes de la inoculacion. Tres de ellos muestran en su historia familiar parientes, tias o tios, con hidrocefalia, fiebre, convulsiones, defectos mentales o epilepsia.

Seis niños reaccionaron explosivamente a la primera dosis, tres a la segunda dosis y seis a la tercera dosis. Tres niños que habian tenido convulsiones en las primeras dosis reaccionaron otra vez con convulsiones en la dosis sucesiva. Las convulsiones fueron en todos los casos el sintoma mas sobresaliente. Despues de la enfermedad aguda un niño tuvo tres convulsiones espaciadas en cinco meses pero durante los dos años siguientes se mantuvo normal. Los catorce niños restantes sufrieron de variados trastornos cerebrales cronicos: dos presentaron signos de demencia marcada en distintos periodos, terminando con la muerte, nueve mostraron una variedad de defectos, deficiencia mental,

epilepsia, paralisis cerebral y tres de ellos han sido observados demasiado recientemente para establecer una conclusion definitiva.

Durante un periodo de diez años, ocho niños con encefalomielitis consecutiva a la vacunacion fueron admitidos en el Hospital de Niños de Boston. Desde que se realiza la vacunacion virtualmente en el 100% de la poblacion, la encefalopatia consecutiva al metodo profilactico de inmunizacion contra la tosferina se observa mas frecuentemente y con mas severidad que en los casos que siguen a la vacunacion antivariolica.

Un importante riesgo de encefalopatia se observa en el uso de la vacunacion profilactica contra la tosferina. En vista de esta posibilidad y de la falta de seguridad absoluta en la eficacia de la vacuna parece que los niños estan sin embargo mas seguros vacunados que no. El presente estudio no llega a dilucidar los medios por los cuales la vacuna daña al tejido nervioso. Grandes esfuerzos para disminuir este azar, ya por modificaciones de la vacuna, o por nuevos metodos en su administracion parecen indicarlo.

319 Longwood Ave.

STOMATITIS IN INFANTS CAUSED BY B. MUCOSUS CAPSULATUS

By ROBERT L. FAUCETT, M.D., AND HERBERT C. MILLER, M.D.
Kansas City, Kan.

DURING the past two and one-half years we have seen six infants with an infection of their mouths which bore some resemblance to thrush but which proved on further study to be different from thrush in its physical appearance, its etiology and in its response to treatment. In all six infants a Gram negative organism probably belonging to the B. mucosus capsulatus group was recovered from the lesions on culture; in three of the infants it was the only organism found, and in the remaining three it was found together with Monilia albicans. The organism was easily seen on smears made directly from the lesions. Despite the difficulty in definitely classifying the organism we feel it is important to record these cases, so that similar cases can be differentiated from thrush and receive the benefits of sulfadiazine treatment.

CLINICAL DESCRIPTION

The physical appearance of the lesions was much the same in all six cases. A photograph of the infected mouth of one of the infants is shown in Fig. 1. The lesions consisted of a dirty white membrane that tended to be confluent but was sometimes patchy, which, when gently scraped, resulted in bleeding from the ulcerated parts beneath the membrane. The lesions were particularly confluent on the dorsal and ventral surfaces of the tongue and gums and usually patchy on the buccal mucous membranes and hard palate. The edges of the lesions were well defined. When healing took place, the involved parts of the mouth returned to normal within a week or ten days. The lesions can be tentatively differentiated from thrush by their greater tendency to be confluent and to have a heavier, dirtier appearing membrane. Cultures and smears are necessary, however, to establish the diagnosis.

Four of the six infants developed lesions during the newborn period, the earliest appearing in one five-day-old infant. All four of these infants were healthy full term infants. Of the remaining two cases one was two months old and had bilateral hydroureters and pyelitis caused by B. pyocyaneus, and the other was 27 months old and had nephrosis.

Direct contact between any of the six infants was not demonstrated, although two of the newborn infants occupied the same nursery in another hospital within ten days of each other. One of these infants was admitted to the University of Kansas Medical Center and was on the same floor and ward as the child with nephrosis, although the latter did not develop stomatitis until 20 days after the discharge of the infant admitted from the outside. The remaining three cases occurred sporadically during the next two years and their infections were apparently unrelated.

There was no systemic response to the infection observed in any of the six infants. There was no fever, vomiting or diarrhea. No abnormal changes were noted in the leucocyte counts. The mouths of these infants seemed to be tender, as the children

From the Department of Pediatrics, University of Kansas School of Medicine, Kansas City, Kan.
(Received for publication January 13, 1948.)

refused to eat well and cried readily. These symptoms disappeared when the infection cleared. One newborn infant in this series was hospitalized because of dehydration, which resulted from an inadequate fluid intake, presumably related to the soreness of the mouth.

The infection was quite resistant to all the usual forms of local treatment used in thrush, including 1% gentian violet, 5% chromic acid and peroxide. Local treat-

FIG. 1. Membranous stomatitis caused by B. mucosus capsulatus involving tongue, gingiva and buccal mucosa.

ment was started on one infant on the seventh day of life and was continued for the next two months with only slight change in the appearance and extent of the lesions. In contrast to the poor response to local applications was the dramatic recovery that occurred when sulfadiazine was given by mouth in doses averaging a grain per pound of body weight per day. One newborn infant treated locally for nine days without benefit showed definite regression of the lesions after 24 hours of sulfadiazine therapy and complete recovery within four days. Cultures from the mouth of this infant were negative for this organism four days after sulfadiazine therapy was started. Similar good clinical results were obtained in the three remaining infants receiving sulfadiazine. Two of the infants in whom the diagnosis was established were not treated with sulfadiazine. The infant with hydroureters and pyelitis had both

Monilia albicans and a Gram negative bacillus on culture of her mouth lesions. Her response to sulfadiazine was less dramatic than the rest. The failure of her mouth to clear completely was thought to be related to the additional infection by Monilia albicans. The good results obtained when sulfadiazine was administered almost certainly were related to the high degree of sensitivity of the bacterial organism to this drug. In vitro tests showed that growth of this organism was inhibited at a concentration of 1.25 mg./cc. of sulfadiazine. Penicillin did not appear to be effective when given parenterally in amounts of 2,000 and 10,000 units intramuscularly to two of the newborn infants with stomatitis over a period of three and four days respectively.

Efforts were made to ascertain the distribution of the organism described in this report. During the period covered by this study, almost two and a half years, bacteriologic studies have been made on 19 cases of thrush on the wards and in the nurseries under the supervision of the Pediatric Service. Monilia albicans was found alone in 12 of these cases and was recovered in the remaining seven cases in conjunction with either Esch. coli, Friedländer's b. or an aerogenes-like organism. In the same period of time there were 1060 nose and throat cultures made on the children and newborn infants admitted to the Pediatric Service because of various infections. In only one case was the organism described in this study recovered in one of these cultures. This was in an infant 14 months old who had a mild pneumonia and no evidence of any lesions in her mouth or pharynx. In this child the organism was recovered from the throat culture. In one of the newborn infants with stomatitis an organism identical with the one from the mouth was recovered from the stools and vagina, although there was no bowel disturbance or lesion in the vagina.

Attempts to classify the organism recovered from these infants were made by several investigators working in different laboratories.* The consensus was that the organism should be classified tentatively in the B. mucosus capsulatus group. The organism did not quell with either Friedländer Type A or Type B Sera. It could not be classified in the aerogenes group. An antiserum made from the organism recovered from the first case agglutinated to a titre of 1-1500 the organisms recovered from two of the remaining five cases. Although similar tests were not done in the other three cases, we can be fairly sure from the morphologic appearance and cultural characteristics that the organism was the same in the remaining three cases.

Comment

We have not been able to discover reports of cases in which either the mouth lesions or the bacteriologic characterizations were like those described here. At first we were skeptical of our own findings, since the organism could not be identified clearly; but as additional cases appeared over a period of two and a half years with exactly the same findings, with the identical organism, and with the same good response to sulfadiazine therapy, our belief that we had a definite entity became more certain. Further support for this belief came from the fact that the organism was recovered in pure culture in three of the cases, and in the remaining three in which Monilia also was recovered there was definite regression of the lesions in those infants receiving sulfadiazine. The fact

* We are indebted to Dr. Noble P. Sherwood, Department of Bacteriology, University of Kansas; Dr. Dwain Walcher, Department of Pediatrics, Yale University and Dr. Herbert Wenner, Department of Pediatrics, University of Kansas, for their attempts to identify this organism.

that this organism was found only in connection with the mouth lesions and not in routine nose and throat cultures offers additional support for believing it was the casual agent in the stomatitis.

An organism classified as B. mucosus capsulatus has recently been reported by Walcher[1] as the probable etiologic agent in several infants who developed diarrhea in an institutional outbreak. A culture of the organism recovered from one of the infants in the present study was sent to Dr. Walcher to determine if it might be similar to the one recovered by him from the infants with diarrhea. He could demonstrate no quelling nor agglutination of our organism with rabbit serum made against the bacillus obtained from the infants with diarrhea.

Summary

Six infants have been reported with an extensive membraneous infection of their mouths caused by an organism belonging to the B. mucosus capsulatus group. The infection failed to respond to local measures, but cleared when sulfadiazine was given in proper dosage.

References

1. Walcher, D. N., B. mucosus capsulatus in infantile diarrhea, J. Clin. Investigation **25**:103, 1946.

Spanish Abstract

Estomatitis en el Niño Causada por el Bacilo Mucosus Capsulatus

Seis casos de estomatitis membranosa, fueron observados en niños menores de dos años. Las lesiones, fueron confundidas al principio con un simple muguet, pero los cultivos demostraron la presencia en todos los casos de un microrganismo que resulto ser el Bacilo Mucosus Capsulatus.

Este germen fue encontrado en cultivos puros en tres de los casos y los tres restantes estaban asociados con la presencia de monilia albicans. Las lesiones de la boca de estos niños desaparecieron dentro del termino de uno a cuatro dias despues de la administracion de sulfadiazina a la dosis de 13 mlgs. por kilo de peso y por dia. Las lesiones de la boca de estos seis niños son muy semejantes a las causadas por la monilia albicans, generalmente presente en los casos de simple muguet siendo naturalmente necesaria la siembra para afirmar el diagnostico bacteriologico unico medio de establecer la diferencia.

Bell Memorial Hospital

MULTIPLE CONGENITAL MALFORMATIONS: A CONSIDERATION OF ETIOLOGIC FACTORS

JOSEF WARKANY, M.D., CAROLYN B. ROTH, AND JAMES G. WILSON, Ph.D.,
Cincinnati, Ohio and Rochester, N.Y.

THE medical literature of the past five decades is replete with statements that multiple congenital malformations are always and necessarily due to changes in the germ plasm. In one sense such statements imply that multiple congenital anomalies are always hereditary and, when so interpreted, they may lead to untoward consequences. It is of considerable practical importance for the bearer of congenital defects, as well as for other members of his family, to know whether or not his defects are heritable. The question is also of concern to those who are sincerely interested in eugenics from the standpoint of public health. The importance of this point is illustrated by a certain sterilization law which was enforced for some time upon 80 million people and which stated: "Persons who show simultaneous appearance of different severe, or even mild physical endogenous malformations . . . . should be sterilized, if in the blood relationship any severe or mild endogenous malformations have been shown to occur in at least one person singly, bilaterally or in aggregation."[1]

The opinion that multiple congenital malformations are necessarily hereditary dates back to the time when amniotic bands were considered the only extrinsic cause of malformations. Since it was difficult to explain familial, symmetrical, systemic or internal malformations in terms of amniotic bands; and, since no other environmental mechanisms capable of producing such malformations had been recognized, these anomalies were attributed to changes in the germ plasm. This is expressed in a textbook on "Human Heredity"[2] in the following words:

"There is hardly a malformation which has not been referred to this cause" (i.e., errors of amniotic development) "including a great many which are beyond question hereditary. If a malformation of the same kind occurs in numerous members of a family, we can say with certainty that it cannot be caused by an error in the development of the amnion. Furthermore, when malformations are symmetrical, there can be little doubt that they are truly hereditary. If, for instance, we find the same malformation in both hands, we can conclude with the greatest probability that the trouble is hereditary. The same thing applies to malformations which exhibit a serial homology, being of the same character both in the hands and in the feet."

There can be no doubt that multiple congenital malformations may be genetically determined and hereditary. It has been repeatedly observed in both man and animals that an abnormal gene with pleiotropic effects, or several such genes in combination, can produce syndromes of multiple malformations. But it is the purpose of this

---

From the Children's Hospital Research Foundation, Department of Pediatrics, College of Medicine, University of Cincinnati and from the Department of Anatomy, School of Medicine and Dentistry, University of Rochester, New York.

Read before the 57th Annual Meeting of the American Pediatric Society in Stockbridge, Mass., May 13, 1947.

This work was aided in part by a grant from the Nutrition Foundation, Inc., New York, N.Y.
(Received for publication January 21, 1948.)

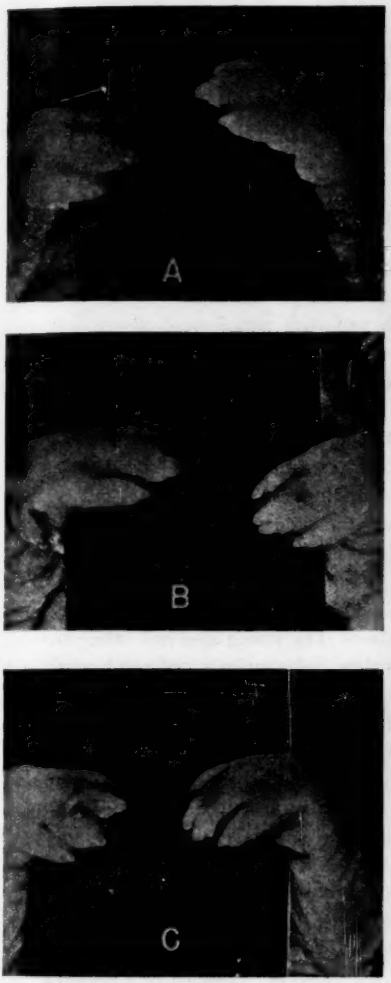


FIG. 1

FIG. 2

FIG. 1. Congenital malformations of forepaws in three newborn rats, littermates, induced by maternal riboflavin deficiency. A. Complete syndactylism of digits III and IV. B. Incomplete syndactylism of digits III and IV. Nails of fused digit are separated. C. On left forepaw fusion of digits III and IV resembles that of B. Terminal phalanges of right forepaw are not fused.

FIG. 2. Congenital malformations of extremities of newborn rats, induced by maternal riboflavin deficiency. Both extremities are shortened and digits III and IV are fused in forepaws as well as in feet.

paper to emphasize the fact that similar syndromes may also be caused by a variety of environmental influences and there is no evidence that such defects are hereditary.

Gregg[8] in 1941 discovered that rubella in the mother may be an etiologic factor in causing congenital cataract and heart disease in the offspring if the infection occurred

during the first three months of pregnancy. Other symptoms included in the syndrome associated with maternal rubella are congenital deafness, mental retardation and malformations of the skull and teeth, although the coexistence of all these anomalies in the same patient is rare. This syndrome affords an example of multiple congenital anomalies resulting from an infectious process which interferes in some way with the normal development of the embryo. Since rubella usually induces permanent immunity, a mother is not likely to have more than one child with the prenatal rubella syndrome. On the other hand, toxoplasmosis may cause congenital anomalies in more than one child in the same family.[4]

Multiple congenital malformations have been induced experimentally in the skeleton of rats by maternal riboflavin deficiency.[5,6] Shortening of the mandible, radius, ulna, tibia and fibula, various forms of syndactylism and cleft palate were observed in the affected young. Fig. 1 shows the forepaws of three newborn littermates whose mother had been reared and bred on a riboflavin-deficient diet. All three young had anomalies of the digits; in two there was symmetrical syndactylism (Fig. 1, A and B) while in the third (Fig. 1, C) the fusion of digits III and IV was less complete on the right than on the left side. In Fig. 2 is shown a newborn rat with shortening and syndactylism of the upper and lower extremities, which exemplifies "serial homology." Thus, familial,* symmetrical and "serially homologous" congenital malformations can be attributed to such an environmental factor as riboflavin deficiency.

Hale[7,8,9] reported manifestations of prenatal vitamin A deficiency in pigs. Gilts fed a vitamin A deficient diet before and during the period of embryonic development gave birth to pigs with anophthalmos or microphthalmos. The young also had other malformations, such as accessory ears, cleft lip and palate, subcutaneous cysts and misplaced kidneys. Hale proved experimentally that genetic factors can be ruled out as the cause of the malformations. Other congenital malformations of nutritional origin, such as syndactylism, talipes, kinked tail and ocular defects were observed in swine by Ross et al.[10]

A syndrome of multiple congenital anomalies in soft-tissue organs can be induced in rats whose mothers are reared and bred on a vitamin A deficient diet. In the newborn young of such mothers congenital anomalies of the eyes have been observed.[11] The most frequent ocular anomaly was a retrolenticular membrane which occupied the place of the vitreous body. Other defects such as folding and coloboma of the retina, rudimentary development of the iris and ciliary body and "open eyes" were also found. The ocular anomalies were usually symmetrical and almost identical in all members of a litter. The striking similarity of these defects in the eyes of siblings is illustrated in Fig. 3, B-F.

Jackson and Kinsey[12] repeated and confirmed these experiments and reported that a maternal vitamin A level of the blood serum under 12 I.U. of vitamin A results in the changes described.

Ocular malformations were the most frequent anomalies found in the offspring of the vitamin A deficient mothers, but many with severely affected eyes revealed in addition developmental defects of other soft tissues. In serial sections of the chest a retardation in development of the pleural cavity and of the lungs was frequently noted.

* The word "familial" is used here as a descriptive term to indicate that an anomaly occurs in several members of a family or a sibship. Repeated appearance of the anomaly in a pedigree may be due to inheritance of abnormal genes in some instances; in others repeated exposure of developing embryos to the same extrinsic adverse factors may also result in a "familial" incidence of anomalies.

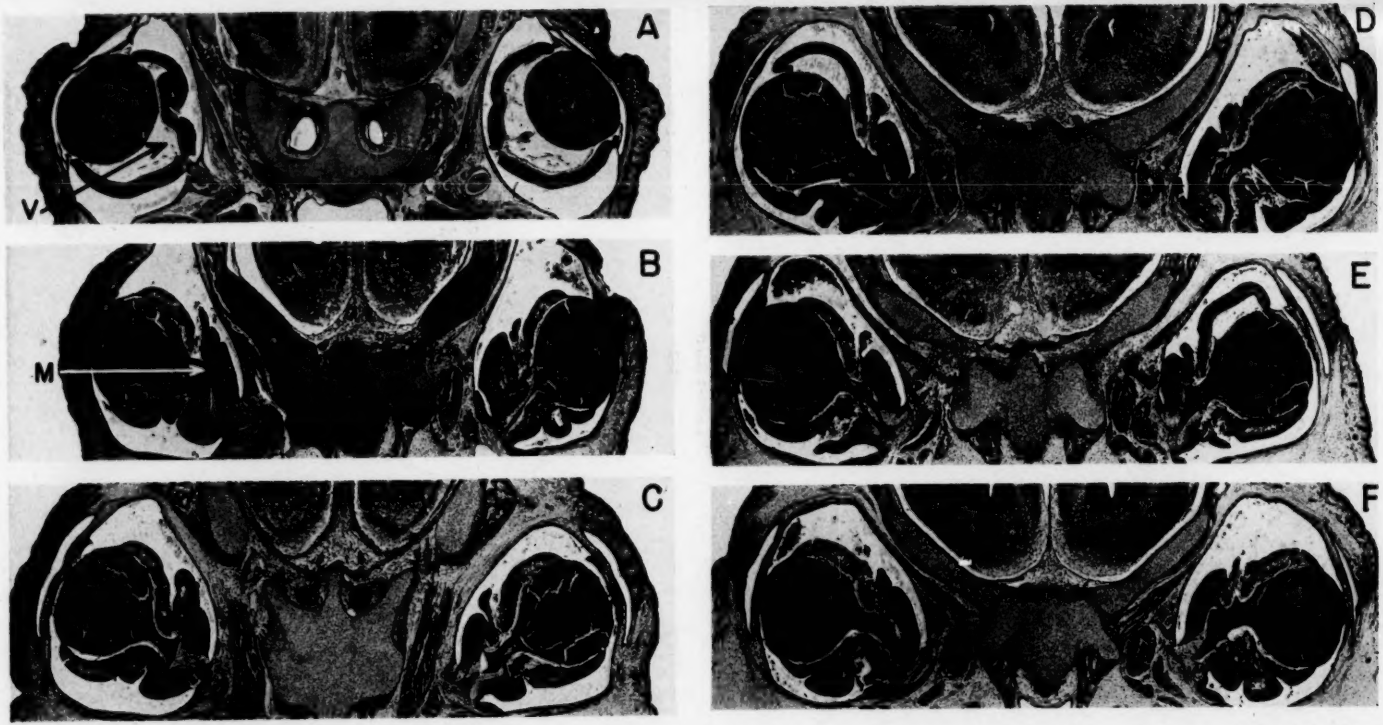


FIG. 3. A. Normal eyes of newborn rat, offspring of a mother fed an adequate diet. Note normal development of corpus vitreum (V) (approx. ×10). B-F. Abnormal eyes of 5 littermates, young of vitamin A deficient mother. All eyes have a retrolenticular membrane (M) in place of corpus vitreum, folding of retina, and rudimentary iris and ciliary body. All eyes, with exception of the right eye in C (on the reader's left) show a coloboma with eversion of retina. (21 day old fetus. approx. ×18).

A peculiar spongy structure of the heart muscle frequently seen in these fetuses at term represents another developmental retardation (Fig. 4, B). In a limited number of fetuses interventricular septal defects were found beyond the age at which this septum normally closes (Table I). There were also various anomalies of the aortic arch, including double arch, right-sided arch and complete absence of the usual fourth arch.[13] Agenesis of one lung and tracheo-esophageal fistula were among the rarer anomalies. Diaphragmatic hernia was found in many of the abnormal young. The right side of the diaphragm was more often affected than the left and in a majority of these cases an accessory lobe of the liver projected into the right pleural cavity (Fig. 4, C). The occurrence of diaphragmatic hernia in the young of rats bred on a diet deficient in vitamin A has been reported also by Anderson.[14] In this respect our experiments confirm Anderson's findings.

Sections through the abdomen and pelvis revealed numerous anomalies in the genito-urinary system. The renal pelvis and the ureters were not dilated (Fig. 5, B) as in the normal (Fig. 5, A) and often the testes were not descended. In some animals the lower poles of the kidneys were fused to form horseshoe kidneys (Fig. 5, C). The Wolffian and Müllerian ducts persisted side by side and the development of the urogenital sinus was retarded.[13] A reconstruction of this region in an abnormal male is shown in Fig. 6. In this instance and several others similar to it the ureters do not terminate in the bladder but join the vas deferens, which constitutes an embryologically primitive type of ectopy of the ureters. The penis was occasionally seen to have the usual urethral orifice and in addition a hypospadiac opening at its base (Fig. 7). All abnormal fetuses of 18 days gestational age or older showed keratinizing metaplasia in epithelia of structures derived from the fetal urogenital sinus. These changes, which are characteristic of vitamin A deficiency in postnatal life, were limited in the fetuses and newborns of vitamin A deficient mothers to the genitourinary tract while the epithelia of other regions were not affected.[15]

The number of animals in this series was limited by the necessity of making serial sections for the recognition of many of these anomalies. The heads of 114 young of vitamin A deficient mothers were sectioned and in 89 abnormal eyes were found. The eyes of 60 control animals, the young of mothers fed an adequate stock diet, were histologically normal. Sixty control animals were dissected and no diaphragmatic hernia and no horseshoe kidney were found.

Identical abnormalities were found in the young of rats obtained from Sprague Dawley in Wisconsin and in rats from the Albino Farms in New Jersey.

Under the experimental conditions employed over 75% of the young have abnormal eyes.[16] Table I lists the frequency of other congenital anomalies in 50 specimens with abnormal eyes. Judged by the severity of the ocular anomalies, the fetuses used in this study included a higher percentage of severely anomalous specimens than the total offspring of the vitamin A deficient mothers. Thus the percental occurrence of the anomalies described in Table I must not be considered as representative of the anomalies of all the young obtained. From an embryologic point of view the more anomalous specimens were more interesting than those with mild changes and, therefore, more of these specimens were included in the study than their actual incidence would afford. Several of the defects listed in Table I represent retarded rather than aberrant development, but for the present purpose there is no necessity to distinguish between them.

Thus two different syndromes of multiple congenital anomalies can be produced

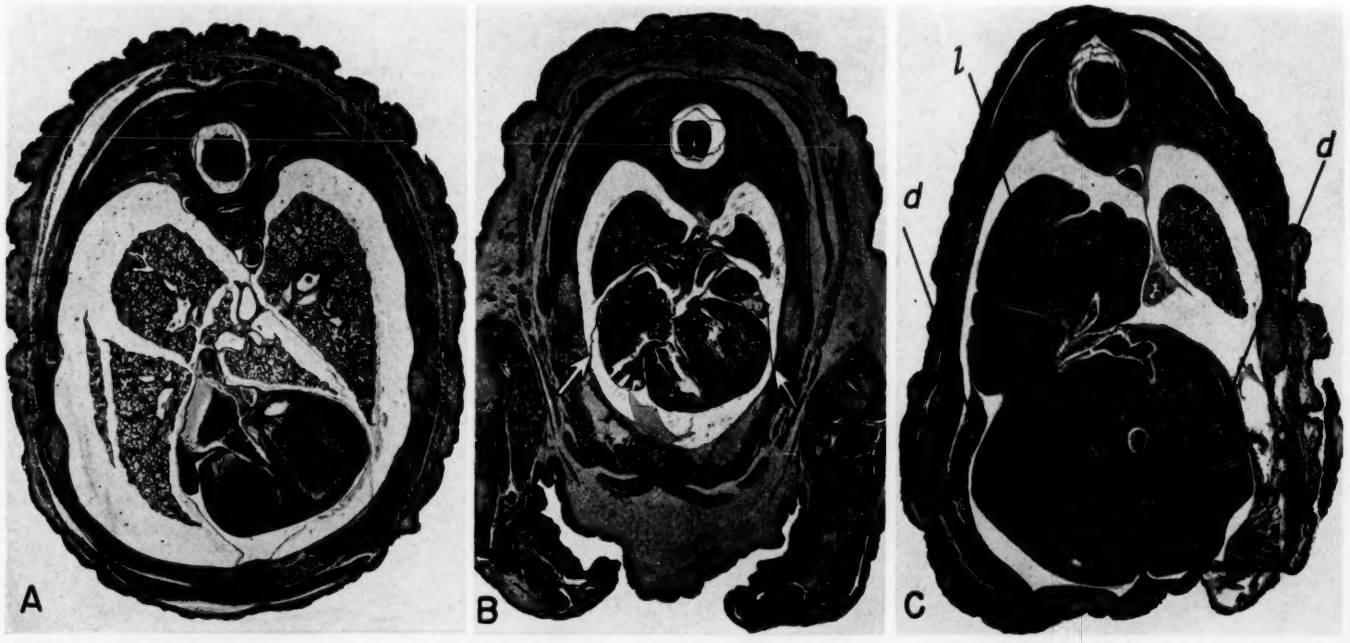


FIG. 4. A. Transverse section through chest of normal newborn rat (approx. ×6⅔). B-C. Transverse sections through abnormal young (22 day old fetuses), offspring of mothers reared and bred on vitamin A deficient diets. B. Arrows indicate ventral borders of pleural cavities. Lungs and pleural cavities are underdeveloped and do not envelop the heart. Heart muscle is "spongy" (×6⅔). C. Diaphragmatic hernia. Diaphragmatic leaves (d) are not connected with one another and an accessory lobe of liver (l) protrudes through opening into right pleural cavity (approx. ×12).

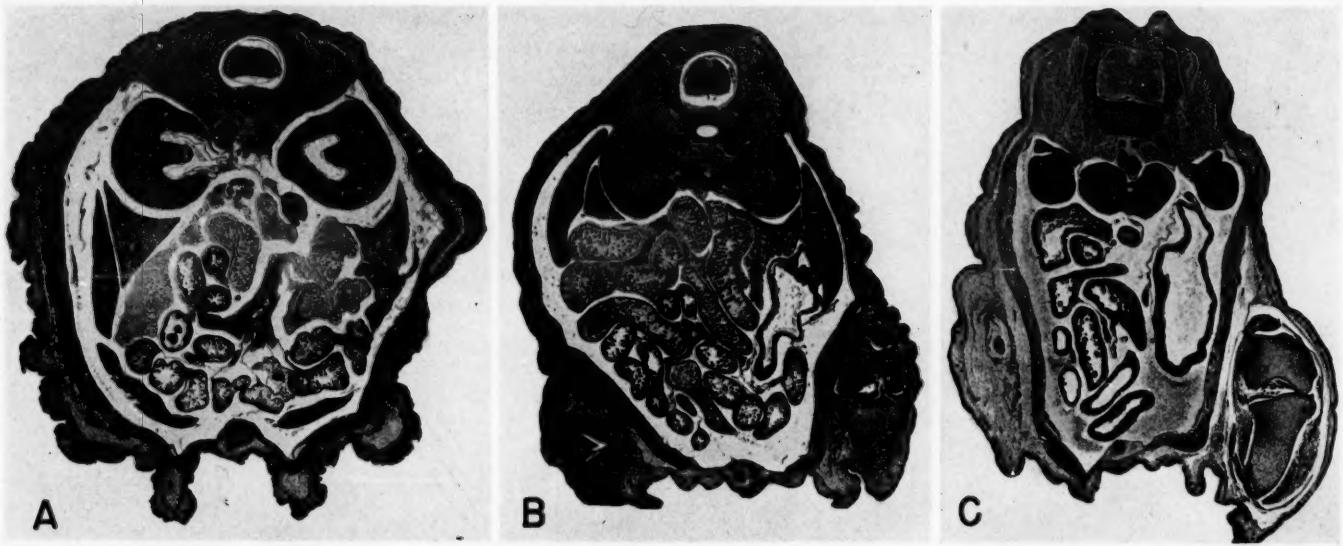


FIG. 5. A. Transverse section through abdomen of normal newborn rat. Note dilated renal pelvis (approx. ×7⅓). B-C. Transverse sections through abnormal young offspring of mothers reared and bred on vitamin A deficient diets. B. Section goes through renal pelves which are not normally dilated (22 day old fetus, ×7⅓). C. Undescended testes are on a level with fused lower poles of kidneys (horseshoe kidney). (20 day fetus, approx. ×10.)

experimentally in the young of female rats reared and bred under adverse environmental conditions: lack of vitamin A or lack of riboflavin in the maternal diet. These syndromes vary in degree and not all abnormal animals show all the anomalies which

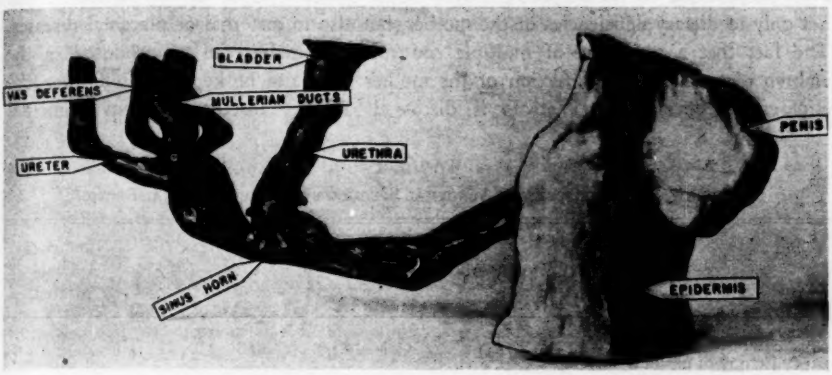


FIG. 6. Wax-model of lower genito-urinary tract of an abnormal, male, new-born rat, offspring of a vitamin A deficient mother. Ureters do not terminate in the bladder but join mesonephric ducts (vasa deferentia) and empty with these directly into urethra (ectopic ureters). There are very few prostatic buds and no seminal vesicles. Müllerian ducts persist.

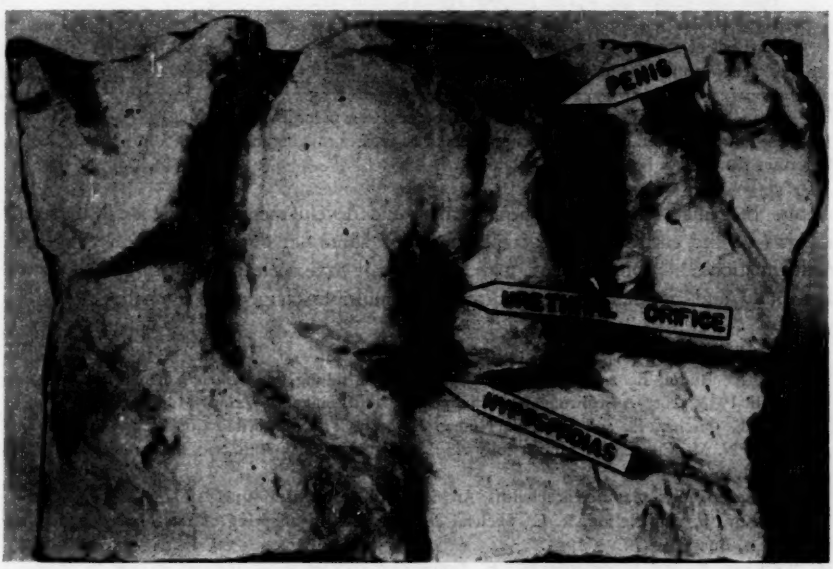


FIG. 7. Ventral view of wax-model reproduced in Fig. 6. Note hypospadias below normal urethral orifice.

constitute the respective syndromes. It may be assumed that some of the most abnormal fetuses die in utero and that the fetuses which reach the end of the gestational period are less severely affected.[16] Anomalies may occur in several members of a family and

they may be symmetrical or "serially homologous." These experiments should make us wary of attributing all types of multiple congenital defects to changes in the germ plasm. It is irrelevant whether dietary conditions comparable to our experiments are ever encountered in human beings. Nutritional deficiencies of the fetus can be due not only to dietary deficiencies of the mother, but also to maternal or placental diseases. The fact that a syndrome of multiple congenital anomalies can be produced in the embryo by an accidental infection of the mother must also be kept in mind when the etiology of developmental errors is discussed. Further instances of environmental

TABLE I

FREQUENCY OF ANOMALIES IN 50 ABNORMAL SPECIMENS* STUDIED IN SERIAL SECTIONS

Organs Affected	Number of Animals Affected
Abnormal eyes	50
Ectopy of ureteral opening	37
Diaphragmatic hernia	30
Horseshoe and fused kidney	29
Renal pelvis undilated (beyond age of normal unfolding)	25
Both sets of genital ducts persist (beyond age of normal regression of one set)	14
Aortic arch anomalies	11
Open interventricular septum (beyond age of normal closure)	10
Hypospadias	7
Agenesis of one lung	5
Tracheo-esophageal fistula	1

* Selected on the basis of abnormalities in the eyes. (See preceding paragraph.)

These data are based on a survey of sections of 34 fetuses ranging in age from 16 to 21 days and of 16 fetuses removed or born on the 22nd day.

factors that may adversely influence embryonic development are discussed in recent reviews of the entire subject of the causes of abnormal development and congenital malformations.[17,18] Difficult as it may be, we shall have to learn to distinguish between hereditary and non-hereditary syndromes of multiple congenital anomalies.

REFERENCES

1. Gütt, A., Rüdin, E., and Ruttke, F., Gesetz zur Verhütung erbkranken Nachwuchses vom 14. Juli 1933 nebst Ausführungsverordnungen, J. F. Lehmanns Verlag, München, 1936.
2. Baur, E., Fischer, E., and Lenz, F., Human Heredity, The Macmillan Co., New York, 1931.
3. Gregg, N. M., Congenital cataract following german measles, Ophth. Soc. Australia, Trans. **3**:35, 1941.
4. Crothers, B., Toxoplasmic encephalitis, Arch. Neurol. & Psychiat. **49**:315, 1943.
5. Warkany, J., and Nelson, R. C., Skeletal abnormalities in offspring of rats reared on deficient diets, Anat. Rec. **79**:83, 1941.
6. Warkany, J., and Schraffenberger, E., Congenital malformations induced in rats by maternal nutritional deficiency; preventive factor, J. Nutrition **27**:477, 1944.
7. Hale, F., Pigs born without eyeballs, J. Heredity **24**:105, 1933.
8. Hale, F., Relation of vitamin A to anophthalmos in pigs, Am. J. Ophth. **18**:1087, 1935.
9. Hale, F., Relation of maternal vitamin A deficiency to microphthalmia in pigs, Texas State J. Med. **33**:228, 1937.

10. Ross, O. B., Phillips, P. H., Bohstedt, G., and Cunha, T. J., Congenital malformations, syndactylism, talipes and paralysis agitans of nutritional origin in swine, J. of Animal Science 3:406, 1944.
11. Warkany, J., and Schraffenberger, E., Congenital malformations induced in rats by maternal vitamin A deficiency; defects of eye, Arch. Ophth. **35**:150, 1946.
12. Jackson, B., and Kinsey, V. E., Relation between maternal vitamin A intake, blood level, and ocular abnormalities in the offspring of rat, Am. J. Ophth. **29**:1234, 1946.
13. Wilson, J. G., and Warkany, J., To be published.
14. Anderson, D., Incidence of congenital diaphragmatic hernia in young of rats bred on diet deficient in vitamin A, Transactions of the Society for Pediatric Research, Annual Meeting, Atlantic City, N.J., May 6, 1941, Am. J. Dis. Child. **61**:888, 1941.
15. Wilson, J. G., and Warkany, J., Epithelial keratinization as evidence of fetal vitamin A deficiency, Proc. Soc. Exp. Biol. and Med. **64**:419, 1947.
16. Warkany, J., and Roth, C. B., Congenital malformations induced in rats by maternal vitamin A deficiency; effect of varying the preparatory diet upon the yield of abnormal young, J. Nutrition, **35**:1, 1948.
17. Gruenwald, P., Mechanisms of abnormal development; causes of abnormal development in embryo, Arch. Path. **44**:398, 1947.
18. Warkany, J., Etiology of congenital malformations. Advances in Pediatrics, Vol. II. Interscience Publishers, Inc., New York, 1947.

SPANISH ABSTRACT

Malformaciones Congenitas Multiples; Consideraciones Etiologicas

Dos sindromes diferentes de malformaciones multiples congenitas pueden ser producidas experimentalmente en determinadas circunstancias en las ratas hembras bajo particulares condiciones ambientales: falta de vitamina A o falta de rivoflobina en la dieta materna. Estos sindromes son variables en grado y no todos los animales en tales condiciones de anormalidad muestran todas las anomalias que constituyen los sindromes respectivos. Puede observarse como alguno de los fetos mas anormales mueren en el utero y que aquellos fetos que llegan al final del periodo de gestacion son menos severamente afectados. Las anomalias pueden ocurrir en varios miembros de una familia pudiendo ser simetricas o seriadamente homologas. Estos experimentos hacen atribuir todos los tipos de multiples defectos congenitos a cambios en el germen plasma. Deficiencias nutricionales de los fetos pueden ser debidas no solamente a deficiencias dieteticas en la madre, sino tambien a enfermedades de la madre o de la placenta.

El hecho que un sindrome de anomalias congenitas multiples pueda ser producido en el embrion por una infeccion accidental de la madre debe tenerse in menti cuando tratamos de discutir el desenvolvimiento etiologico. Ademas los factores ambientales que pueden influir adversamente en el desarrollo embriologico son discutidos en reciente revista sobre la materia en que se agrupan las distintas causas de anormal desarrollo y malformaciones congenitas. Estas dificultades nos haran aprender a distinguir entre los sindromes hereditarios y no hereditarios de las malformaciones congenitas multiples.

Elland and Bethesda Ave., Cincinnati
260 Crittenden Blvd., Rochester

MYASTHENIA GRAVIS IN YOUNG CHILDREN

Report of Three Cases—One Congenital

By J. ROBERT BOWMAN, M.D.
Johnson City, Tenn.

MYASTHENIA GRAVIS is seen occasionally in adults, uncommonly in adolescents, and rarely in infants and young children.

Levethan, Fried, and Madonick[1] were able to collect from the literature 34 cases under 17 years with only 8 occurring in children under 10 years of age. They reported an additional case in a nine year old girl whose symptoms began 16 months earlier. Kawaichi and Ito[2] reported a case of a 21 months old boy who developed the disease a month previously. Strickroot, Schaeffer, and Bergo[3] reported a case occurring in an infant born of a myasthenic mother: the infant, on the third day of life, experienced difficulty in taking her formula, and on the fourth day her face grew mask-like, the lower jaw sagged, and dysphagia was noted. When prostigmin was administered her face soon became animated and she was able to nurse normally. Another case, a five year old negro boy, with an acute fulminating onset of dysphagia, dysarthria, ptosis, and respiratory distress, was described by Lieberman.[4] Yahr and Davis,[5] recounted the case of a seven year old girl in whom the symptoms first appeared at about the second year. Ford[6] stated, "In the last few years we have studied seven cases of this disease in children between the ages of eighteen months and ten years," and he reported a ten year old girl who developed ptosis and diplopia at the age of six years.

During the past three years, three children, ages $3\frac{7}{12}$, $4\frac{6}{12}$, and $8\frac{2}{12}$ years, with myasthenia gravis have been treated at the Boston Children's Hospital. These cases are being reported because of the rarity of the disease in children so young, and particularly since myasthenic symptoms and signs were evident in one child at birth.

CASE REPORTS

Case 1. J.D., a white male, age 3 7/12 years, was admitted with the complaints: (1) drooping eyelids since birth, (2) weak voice since birth, (3) increasing fatigability since the age of two years, and (4) cold in the nose with a chronic cough since the age of six months.

The parents and two siblings were healthy and normal. The birth record was normal. He sat alone at about 6 months, walked at 13 months, and talked at 18 months. His mother thought his mental development had been normal, but considered him retarded physically. Even though immunizations against pertussis and diphtheria were given at six months, he developed a severe case of pertussis at ten months. He had measles when 2 6/12 years old. The child had been placed on the waiting list for plastic repair of bilateral congenital ptosis of the eyelids of an outside clinic.

History of the present illness dated from birth, at which time he was observed to have drooping eyelids, and his cry was barely audible. He nursed and swallowed normally. The drooping of the eyelids progressively increased until at the age of four months he appeared "sleepy" all the time, except immediately after naps when he was able to open his eyes widely. His voice was stronger at these times also. The mother always had him photographed in the early morning or following the afternoon nap "because his eyelids drooped less and his face showed more animation" (Figures 1 and 2).

At the age of six months, he caught a "head cold" and this was followed by a cough, both of

From Surgical Service, The Children's Hospital, Boston, Mass., and Department of Surgery, Harvard Medical School.

(Received for publication November 24, 1947.)

which persisted in varying degrees since. "His cough always seemed weak and ineffectual." Pneumonia developed at 13 months of age and was complicated by four generalized convulsions. After the latter, he swallowed with difficulty and liquids regurgitated through the nostrils. Dysphagia continued until he was 20 months old.

When he was about two years old, the mother first observed increased fatigability on walking or playing. "He could walk about a block before tiring and required a prolonged rest period before continuing or was carried." He never had been able to "keep up with the other children; often stopping play before noon and requesting that he be put to bed." Fatigability had increased progressively until at the time he was brought to the hospital, he barely was able to climb a flight of stairs.

On physical examination the boy appeared to be small for his age of 3 7/12 years. He weighed

FIG. 1. Case 1. Photograph, taken after a nap, at about five or six months of age, showing ptosis and sagging of the corners of the mouth.

FIG. 2. Case 1. Photograph, following the afternoon nap, at 13 months.

15.5 kg. and was 109 cm. tall. His appearance was that of a lethargic child who moved about weakly and slowly. Drooping of the eyelids was marked and his face lacked animation. The corners of the mouth sagged, phonation was weak, and the voice had a nasal quality. The eyelids drooped so that about one-half of each iris was covered. Extra-ocular movements were practically absent, and there was little or no lateral or upward gaze. The child held his head back and furrowed the brow and forehead in order to see. The pupils were large and reacted well to light and on accommodation, and seemed not to fatigue. Both fundi were normal.

Pallor and bogginess of the nasal mucous membrane and turbinates were marked. A copious mucopurulent postnasal drip was present, and considerable hyperplasia of the nasopharyngeal lymphoid tissue was noted. The tonsils were enlarged three plus. Contraction of the palate was equal and forceful. The larynx and vocal cords were normal although abduction of the latter seemed weak. Definite weakness and increased fatigability of the anterior neck muscles were elicited. Examination of the abdomen revealed some weakness of the muscles in which fatigue was readily induced by exercise. The extremities showed no deformity, atrophy or paralysis. The muscle mass was adequate and the tone normal. Fatigability of the upper and lower extremities was increased.

Neurologic appraisal was normal, except for the drooping eyelids, the weak extra-ocular movements, bilateral facial weakness, and increased fatigability of the muscles of the anterior neck, the

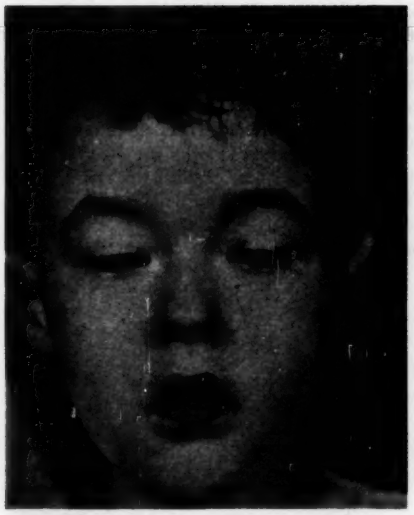


FIG. 3. Case 1. Photograph preceding the "prostigmin test."

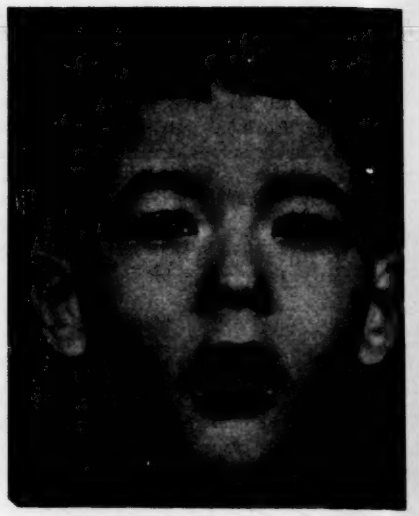


FIG. 4. Case 1. Photograph taken 15 minutes after the injection of 0.3 mg. of prostigmin methylsulfate.

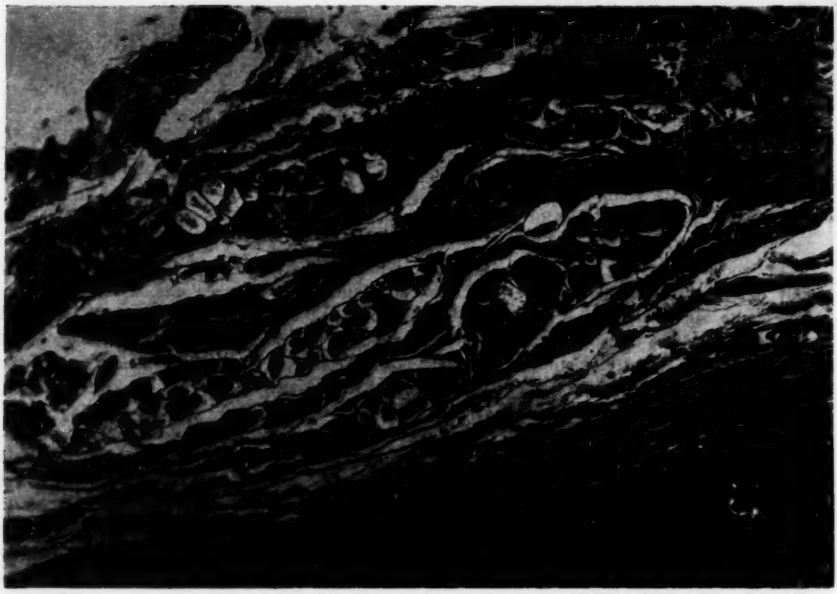


FIG. 5. Case 1. Photomicrograph (H. & E. ×100) of striated muscle biopsied from the anterior pillar of the tonsil, showing atrophy of the muscle fibers.

abdomen, and of the extremities. The reflexes were active, the senses intact, and the sensorium clear. The gait was that of a weak child.

Laboratory data were essentially normal.

Roentgenograms: There was cloudiness of the right ethmoid and right maxillary sinuses, swelling of the nasal turbinates, and hypertrophy of the adenoid tissue. The lungs showed considerable accentuation of the bronchovascular and finer pulmonary markings. There was nothing to suggest a mass lesion in the mediastinum or thymus.

Hospital course: Immediately following admission to the hospital, the child was given 0.3 mg.

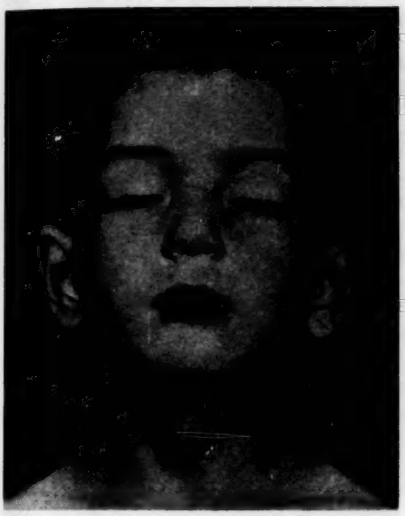


FIG. 6. Case 2. Photograph immediately preceding the "prostigmin test."

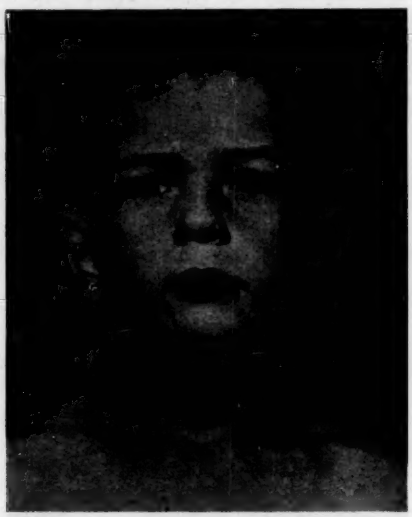


FIG. 7. Case 2. Photograph 15 minutes after the injection of 0.3 mg. of prostigmin methylsulfate.

prostigmin methylsulfate and 0.186 mg. atropine sulfate intramuscularly. Fifteen minutes later (Figures 3 and 4) his face became animated, the eyelids raised, and the voice grew stronger, muscle weakness disappeared, and he was able to play vigorously about the ward.

Myasthenic symptoms recurred on withdrawing prostigmin therapy and subsided when it was resumed. The child was maintained on a regimen of 30 mg. prostigmin bromide every three hours by mouth.

He underwent a tonsillectomy and adenoidectomy without incident. Portions of the anterior pillars were saved for muscle biopsy.

The pathology report was as follows (Fig. 5): "The very few striated muscle fibers which are present show considerable variation in size. The majority of them are small and are separated from one another by large empty spaces. A number of such spaces contain an acidophilic amorphous material, and have the appearance of loss of muscle fibers. Groups of muscle fibers, showing degeneration and atrophy, are often separated from one another by abundant connective tissue containing a very rare fat cell. No lymphocytic infiltrate is demonstrable in the striated muscle fibers or their surrounding connective tissue."

Subsequent visits after discharge from the hospital showed him steadily improving. He had gained weight, was playing actively, and had not had the respiratory infections which had plagued him most of his life. When tired, there still was some ptosis but the mother considered the myasthenic symptoms markedly improved.

Case 2. P.L., a 4 6/12 year old white male was first seen in the Plastic Clinic with the complaint of drooping eyelids, for the past 16 months.

The parents and two sibling were healthy and normal. A cousin (Case 3) had myasthenia gravis. Birth record was normal. Development was slightly retarded in some respects; he held his head erect at 4 months, sat alone at 10 months, walked and talked at 18 months. His mental and physical development had been within the normal range. He had had no diseases other than a few attacks of tonsillitis and cervical adenitis during the third year. At that time the tonsils were removed, but because of "respiratory collapse during anesthesia" the adenoids were left intact.

The present illness began at the age of 3 2/12 years (16 months previous to admission) when the parents first observed drooping of the eyelids, "sadness of the face," weakness of the voice, and increasing fatigability. These symptoms were minimal in the early morning or after sleeping, and grew progressively more marked during the day. The child frequently fell, seemed awkward, and was

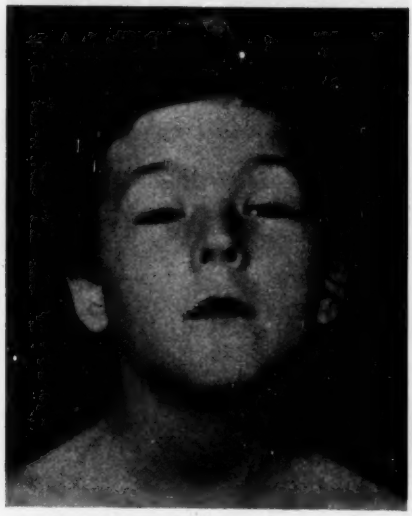


FIG. 8. Case 3. Photograph preceding "prostigmin test."

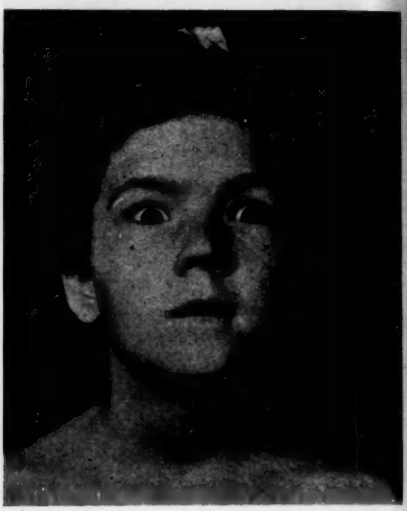


FIG. 9. Case 3. Photograph taken 15 minutes after the injection of 0.4 mg. of prostigmin methylsulfate.

unable to keep pace with the play of other children. No swallowing difficulties or respiratory distress had been experienced.

On physical examination, the boy was small. He weighed 15.5 kg. and was 107 cm. tall. There was marked drooping of the eyelids and his face wore a sad expression because of the sagging facial muscles. The gait was normal but the child moved slowly as if weak. The voice had a slight nasal quality. The eyes showed marked drooping; about three-quarters of each iris was covered. The extra-ocular movements were almost absent. The pupils were quite large and responded well to light and on accommodation and seemed not to fatigue. The fundi were not remarkable. The muscles showed good tone and there was no evidence of paralysis, though the anterior neck group was slightly weak. Increased fatigability of the muscles of the extremities was noted. A roentgenogram of the chest showed no essential variation from the normal.

Because of the appearance of the child with drooping eyelids, muscle weakness, and increased fatigability, myasthenia gravis was suspected. He was given 0.3 mg. prostigmin methylsulfate intramuscularly and 15 minutes later (Figures 6 and 7) had changed from a weak, drowsy-appearing child with drooping eyelids, to a wide-eyed, alert, vigorous boy. He was placed on a regimen of 30 mg. prostigmin bromide every three hours during the daytime and since had been stronger, more alert, and had gained weight steadily; and the myasthenic symptoms and signs had been minimal.

Case 3. M.M., an 8 2/12 year old white girl was seen in the Surgical Out-patient Department. She was brought to the clinic because she had symptoms similar to those of her cousin (Case 2).

The family and past histories were irrelevant; the parents observed "drooping of the eyelids and sagging of the muscles of the face, which caused her to have a sad expression, at the age of 4 years." The voice, since birth, had been soft. She always seemed tired and was unable to play vigorously with other children. Her mother stated, "Her eyes are wide open on awakening in the morning and gradually droop during the day; occasionally they droop, then open widely, especially after naps." There had been no dysphagia or respiratory symptoms. She had developed normally.

The physical examination revealed a tall, slender, girl who weighed 25.9 kg. and was 130.5 cm. tall. There was marked drooping of the eyelids and sagging of the corners of the mouth. The face was sad, lacked animation, and the normal folds were practically obliterated. The eyes were about half covered by the drooping lids. The range of motion of the extra-ocular muscles was markedly diminished in all planes. The pupils were moderately large but responded well to light and on accommodation, and showed no fatigue on repeated stimulation. Although the palate contracted normally, the voice had a slight nasal quality; but phonation was strong.

The extremities were well developed, the muscles had good tone, and no definite weakness or increase fatigability could be elicited.

A roentgenogram of the chest was normal.

Since the findings appeared to be consistent with a diagnosis of myasthenia gravis, the child was given the "prostigmin test" (Figures 8 and 9) —0.4 mg. prostigmin methylsulfate intramuscularly. After 15 minutes all the myasthenic symptoms and signs had subsided and disappeared.

The child was maintained on 30 mg. prostigmin bromide every three hours orally, and showed remarkable improvement.

SUMMARY

Three cases of myasthenia gravis occurring in young children have been presented.

All infants and children having ptosis of the eyelids should be given the "prostigmin test."

Myasthenic symptoms and signs were evident at birth in Case I, and this is the first case of congenital myasthenia gravis to be reported in the medical literature.

REFERENCES

1. Levethan, S. T., Fried, A. J., and Madonick, M. J., Myasthenia gravis, prostigmin methyl-sulfate used, Am. J. Dis. Child. **61**:770, 1941.
2. Kawaichi, G. K., and Ito, P. K., Myasthenia gravis, Am. J. Dis. Child. **63**:354, 1942.
3. Strickroot, F. L., Schaeffer, R. L., and Bergo, H. L., Myasthenia gravis occurring in infant born of myasthenic mother, J.A.M.A. **120**:1207, 1942.
4. Lieberman, A. T., Myasthenia gravis with acute fulminating onset, J.A.M.A., **120**:1209, 1942.
5. Yahr, M.D., and Davis, T. K., Myasthenia gravis, J. Pediat., **25**:218, 1944.
6. Ford, F. R., Diseases of the Nervous System in Infancy, Childhood, and Adolescence, Second Edition, Charles C Thomas, Springfield, Ill., 1944, p. 1030.

SPANISH ABSTRACT

Reporter de Tres Caso de Miastenia Grave en Niños Pequeños, Uno de Ellos Congenito

Se han reportado catorce casos de miastenia grave en niños menores de 10 años. Durante los ultimos tres años tres niños de tres años y siete meses, cuatro años y seis meses y ocho años y dos meses, con miastenia grave fueron tratados en el Hospital de Niños de Boston. Estos casos fueron reportados por la rareza de la enfermedad en niños tan jovenes y particularmente porque la evidencia de la miastenia fue comprobada en uno de ellos en el nacimiento. Disfagia consecutiva a un severo ataque de bronconeumonia a la edad de trece meses. Debilidad muscular mas o menos generalizada y un aumento gradual de fatigabilidad se desarrollo. Este niño, al igual que los otros dos mostro una miastenia tipica que respondio a la prostigmina y mejoro rapidamente cuando fue colocado en un regimen de neostigmino-terapia. Fotografias antes y despues de la prueba de prostigmina se acompañan en el reporter. Todos los niños presentaron ptosis del parpado y fueron sometidos a la prueba de la prostigmina. El caso 1 ha sido el primero reportado de miastenia grave congenita.

610 Hamilton National Bank Bldg.

TOXOPLASMIC ENCEPHALOMYELITIS

A Clinical Report of Six Cases

By GABRIEL A. SCHWARZ, M.D., ELIZABETH KIRK ROSE, M.D., AND WILFRED E. FRY, M.D.
Philadelphia, Pa.

THROUGH the brilliant pioneer work of Wolf, Cowen and Paige, the protozoan parasite of rodents and birds, the Toxoplasma, has been proven to invade the central nervous system of human infants. Subsequently, this organism was found to cause an encephalitis in children and a generalized infection with pneumonitis in adults. Many important facts pertaining to human toxoplasmosis are still unknown, yet from the pathologic observations in infants and children a clinical syndrome has become recognized. It is our opinion that toxoplasmic encephalitis in infants and children can be diagnosed on clinical grounds alone. In support of this contention, we should like to present six cases of this condition seen in private practice and in the wards of the Hospital of the University of Pennsylvania during the past several years.

CASE REPORTS

Case 1. M.S., a white female aged five years, was referred to one of us (G.S.) by Dr. L. T. Chylack of Allentown, Pa., with the chief complaint of partial blindness and abnormal movements of the eyes. She was said to have been normal and well until the age of nine weeks when she was said to have contracted "pneumonia." She had a rather severe febrile illness at this time and was also supposed to have had "pleurisy" as a complication. Unfortunately, no more accurate data are available concerning the nature or extent of this illness. On recovery, she was noted to have abnormal movements of her eyeballs. The mother is of the opinion that the child "was not blind until she was two years of age."

The patient was a full-term infant, born of short labor and without the use of instruments. She began to walk and to talk at the age of three years. At the same age, she is said to have had a convulsion. This attack came on in the evening after supper and lasted for one half hour. The mother had noted that whenever the child was excited her head would shake and her upper extremities were held out in a peculiar fashion. She had had a mild case of measles and of pertussis.

The mother and father were alive and well. There were two healthy siblings. There was no family history of nervous disease or convulsions.

Examination: She was very active and restless. She seemed friendly but was only fairly cooperative. She was exceedingly curious about her environment and wandered about looking closely at all available objects. She had to bring the objects close in order to see them, tilting her head variably as she attempted to see the objects. She presented an unusual type of hyperkinesia. Her movements were somewhat jerky but there was no true incoordination. The child understood what was said to her and carried out simple commands. She spoke well for a child of five. It was estimated that she was of low average intelligence.

She showed no abnormality of station or gait. Romberg test was negative. There were no disturbances in non-equilibratory coordination tests. Sensory system was not fully investigated because of the limited cooperation of the child, but there seemed to be no evidence of change in perception of touch, pain and vibratory sense. She showed continuous rapid, wide and irregular movements of her eyeballs. Voluntary movements of the eyeballs were complete. Pupils were almost equal and reacted well to light. Other cranial nerves were intact. There were no changes in muscle volume, tone or power. All of the deep and superficial reflexes were present, equal and active. There were no pathologic reflexes. General systemic examination showed no abnormalities.

From the Departments of Neurology, Pediatrics and Ophthalmology, School of Medicine, University of Pennsylvania, Philadelphia, Pa.

(Received for publication January 29, 1948.)

Laboratory studies: Blood count showed a hemoglobin of 12.5 gm. and 8700 WBC. Urinalysis was negative. Serologic tests for syphilis were negative. Cerebrospinal fluid was clear and under normal pressure. It contained three cells and a protein value of 12 mg./100 cc. fluid. It gave negative tests for syphilis and the colloidal gold test read 0000000000. Roentgenogram of the skull (Fig. 1) showed small irregular calcifications scattered throughout the brain, but more marked in the occipito-parietal regions. Pneumoencephalogram showed all ventricles to be moderately dilated, as were the basal cisternae. Little air was noted in the cortical subarachnoid pathways.

Ophthalmologic examination: "The media in both eyes is clear. The discs are of normal size and shape and are well outlined. Both discs are pale white. No elevation or edema of the nerve

FIG. 1. Case 1. Pneumoencephalogram showing multiple areas of calcification, especially in the occipito-parietal region. There is moderate dilatation of all the ventricles and the basal cisternae.

heads noted. The arteries appear slightly attenuated. No areas of local constriction seen. Both macular areas are occupied by a large lesion four to six disc diameters in size. The areas are irregularly round and appear white with margins of black pigment. Pigment is also scattered diffusely throughout the atrophic areas. Several choroidal vessels are seen coursing through the atrophic areas. In addition to the macular lesions, several other smaller but similar areas are scattered in the peripheral portions of both retinae."

Serum neutralization test: Blood serum contained neutralizing antibodies for Toxoplasma.

Summary: This five-year-old, white female had a febrile illness diagnosed as "pneumonia" at the age of nine weeks. She had one convulsion at the age of three. She was mentally retarded; partially blind with marked "ocular nystagmus" and torticollis; and had bilateral primary optic atrophy and chorioretinitis especially involving the macular areas. There was a communicating hydrocephalus and multiple intracerebral calcifications. She presented a general motor restlessness and mild hyperkinetic state. Neutralizing antibodies for Toxoplasma were found in her blood serum.

Case 2. T.P., a five-year-old white female, was admitted to the Orthopedic Service at the Hospital of the University of Pennsylvania. She did not walk until the age of three years when it

was noted that she had a waddling gait and an unusual posture of her trunk. Her feet turned outward. Despite these defects, she was very active and could ride a tricycle. She was found to have congenitally dislocated hips and was receiving appropriate treatment for this when her other features were observed.

She was born slightly before term, and was said to have had some respiratory difficulty at birth and remained in a hospital for two months. There was no jaundice. She began to play with toys at six months. She had her first tooth at seven or eight months; sat up at one year; and first talked at two and one-half to three years of age. She had always been "cross-eyed." Her general development was always held by the family to be slower than that of her siblings.

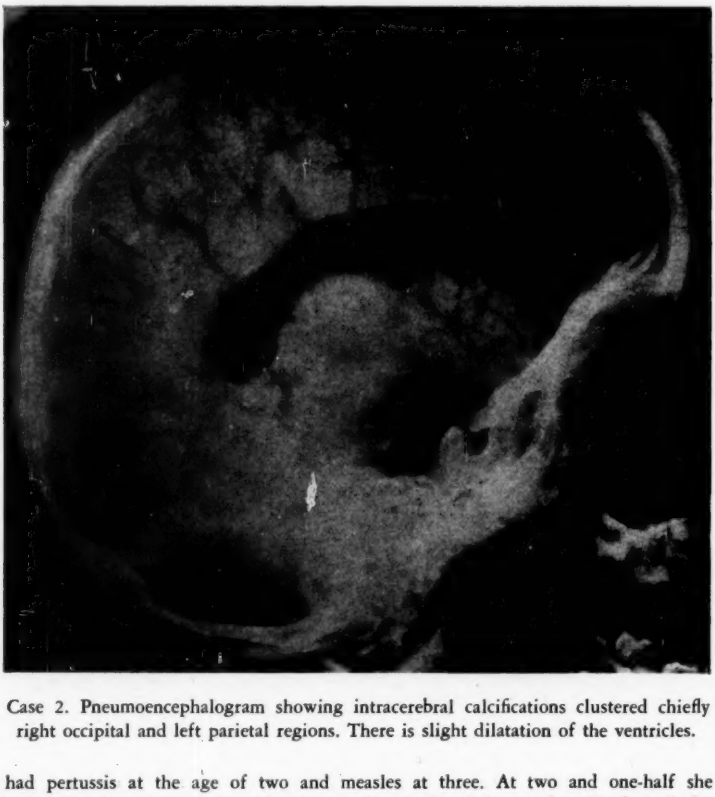


FIG. 2. Case 2. Pneumoencephalogram showing intracerebral calcifications clustered chiefly in the right occipital and left parietal regions. There is slight dilatation of the ventricles.

She had pertussis at the age of two and measles at three. At two and one-half she had a generalized convulsive seizure lasting six minutes. At the age of three and one-half she had a second generalized seizure which lasted one-half hour. Both of these were accompanied by high fever.

Two siblings, brothers, and her parents were in good health. There were no family illnesses.

Examination: She was somewhat pale, but was fairly well nourished. She was about the average size for her age. The head was dolichocephalic and symmetrical. She presented physical signs indicative of bilateral congenital dislocation of the hips. The remainder of the general physical examination was negative. She cooperated poorly and exhibited very little interest in her environment. It was felt that she was mentally retarded. She had fairly well-developed speech. She carried out simple commands fairly well but was readily distracted.

Vision was poor. Her eyes showed a continuous, irregular oscillation. She seemed to fix with either eye. Voluntary movements of the eyeballs seemed to be normal. Pupils were equal and reacted well to light and in accommodation-convergence. Other cranial nerves seemed to be intact. Gait and station were not unusual, except for the defects described above. Romberg test was

negative. Non-equilibratory coordination tests were well performed, although she did seem to have a slight action tremor of her left upper extremity. Muscle power, tone and volume seemed normal. There were no apparent defects in the sensory system. All of the deep and superficial reflexes were obtained. There were no pathologic reflexes.

Laboratory studies: Blood count and urinalysis were well within normal limits. Blood serologic tests for syphilis were negative. Cerebrospinal fluid was under normal pressure. It was clear and contained ten cells. The protein was 27 mg./100 cc. fluid. The test for syphilis and colloidal gold test were negative. Skull roentgenogram (Fig. 2) showed small calcifications in the posterior part of the brain. These were "clustered in two main groups, one in the left parietal region and one in the right occipital region." Pneumoencephalogram showed a slight dilatation of the ventricular system. There was no displacement of the ventricles. Basal cisternae were top normal in size. Cortical and subarachnoid pathways were normal in appearance for the most part, although it was felt that a few might have been widened.

Ophthalmologic examination: "The external examination of the eye is negative except for an ocular type of nystagmus. Visual acuity is limited to light perception. The media are clear. The discs are pale, almost white. There are no exudates or hemorrhages. In each macular region is a large patch of scattered black pigment on a white background."

Serum neutralization test: Positive for toxoplasma.

Summary: This five-year-old white female had a respiratory disturbance at birth. She had some difficulty with her eyes in infancy and had an abnormal gait. She had a history of having had two convulsions. She was found to have bilateral congenital dislocations of the hips and was mentally retarded. She was partially blind, had "ocular nystagmus" and bilateral optic atrophy with areas of degeneration in both macular areas. There were multiple intracerebral calcifications and a moderate dilatation of the cerebral ventricular system. The blood serum contained neutralizing antibodies for Toxoplasma.

Case 3. R.N., a white male, aged five and one-half years, was referred to one of us (G.S.) by Dr. Paul Ramer of Allentown, Pa., because of an enlarged head, retardation and restlessness. He was born after a full-term, uneventful pregnancy. His mother and father were healthy; there were no siblings. He weighed 2,150 gms. at birth and had some difficulty in feeding. He sat up at the age of six months, talked at the age of one and walked when he was two years old. He had had none of the childhood diseases.

At one year, the parents noted that his eyes moved irregularly and he seemed to have difficulty in focusing his eyes on objects. He occasionally tripped over obvious articles and was slow to note objects given to him. His head always seemed to be somewhat enlarged. At about the age of one, he developed wheezy respirations and a cough. On several occasions following these wheezy respirations, he turned blue and showed sternal retraction with labored breathing. About the age of three to four months, the child developed weeping, crusting lesions over the skin of most of the body. This was diagnosed as "eczema" and on appropriate treatment the skin disturbance cleared up and has remained well. Since the age of one year, the patient has had attacks of "asthma" every two or three months.

Examination: The patient seemed small for six years. He was poorly cooperative and showed little interest in his environment. He was able to perform simple commands and seemed to comprehend most of what was said to him. He was able to talk fairly well. It was felt that he was mentally retarded. Head circumference was 49.5 cm. and was symmetrical but there were prominent frontal bosses.

His gait was unsteady. He tended to hold on to nearby objects rather than walk or stand alone. There was some swaying in the Romberg position. Non-equilibratory coordination tests were not satisfactorily performed. There seemed to be no disturbance of an obvious sort in the sensory system. He was partially blind and there were wide, irregular, oscillating movements of the eyeballs. The child could voluntarily move his eyeballs fully. Pupils were rather large and reacted poorly to light. Other cranial nerves seemed to be intact. Muscle power, tone and volume seemed to be normal throughout. All of the deep and superficial reflexes were present, active and equal. There were no pathologic reflexes.

General systemic examination was negative except for right cryptorchidism.

Laboratory studies: Blood count showed a hemoglobin of 10.8 gm., 8600 WBC of which 29% were polynuclear leucocytes, 53% were lymphocytes, and 18% eosinophiles. Blood urea nitrogen

was 15 mg./100 cc. blood and the fasting blood sugar was 15 mg./100 cc. blood. Urine was normal. Blood Kolmer and Kline tests were negative. Cerebrospinal fluid was under normal pressure and was blood-tinged. Fluid contained many red blood cells and a few white blood cells, protein 96 mg./100 cc. fluid, a negative test for syphilis and a colloidal gold curve which read 0000000000.

Skull roentgenograms showed a symmetric enlargement with increased prominence of the digital markings. Sutures were not widened and the sella turcica appeared normal. Chest roentgenogram revealed an accessory lobe in the right base. Two pneumoencephalograms were attempted by the lumbar route and one by the cisternal. These were unsuccessful. Ventriculogram (Fig. 3) showed a

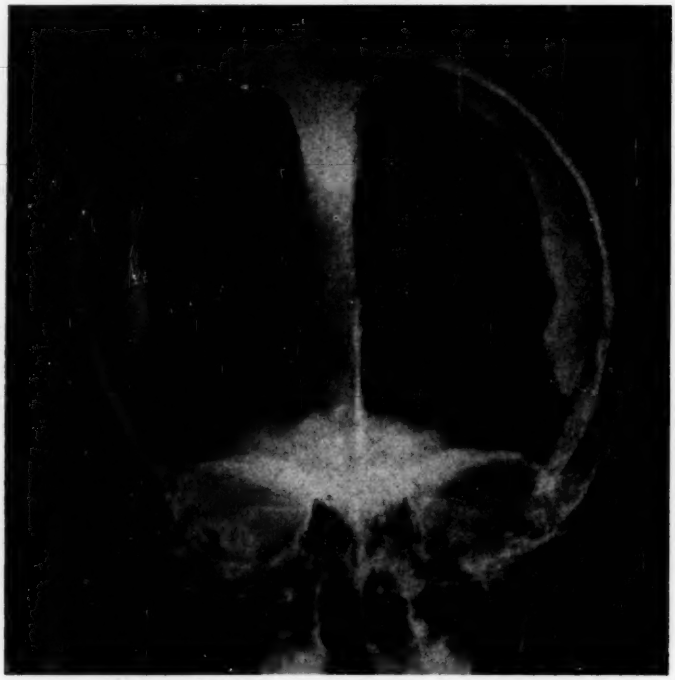


FIG. 3. Case 3. Ventriculogram showing marked dilatation of the lateral ventricles and a dilated cyst of the septum pellicidum.

marked dilatation of the lateral ventricles. There was a dilated cyst of the septum pellucidum. The third ventricle, aqueduct of Sylvius and fourth ventricle were not seen. It was felt that this picture was the result of a block of the foramen of Munro or just below it.

Ophthalmologic examination: The fundi were examined under avertin anesthesia: "In the right eye, the lens was clear except for a Mittendorf dot on the posterior surface of the capsule with a remnant of the hyaloid attached to it and extending about one-third of the way back into the vitreous. The vitreous was filled with many fine dust-like, stringy opacities. The fundus was about nine diopters myopic. The optic disc showed some blurring of the margin. The color was gray-pink. The surface markings were rather indistinct. There was no measurable elevation of the disc. The retinal arteries and veins were narrower than normal. The retina nasal to the disc appeared essentially normal until the mid-periphery was revealed. Here, large white areas of chorioretinal atrophy with marked pigment migration began to appear and extended peripherally as far as could be followed. Similar areas, varying in size from smaller than the disc to ten times or

more the size of the disc appeared above, below and temporally. There was one particularly large area in the macular region itself. Small areas of retina between the areas of atrophy were essentially normal except for an occasional scattering of retinal pigment. Several sites in the atrophic areas showed not only pigment disturbance but also proliferative changes consisting of fibrous bands. There were no fresh exudates, hemorrhages or edema seen anywhere.

In the left eye, the lens appeared normal. The vitreous showed fine opacities as were seen in the right eye. The fundus was about the same degree myopic as on the right side. There was chorioretinal atrophy of almost all the whole side of the nasal fundus, extending far into the periphery. Above and below the disc, there were five or six lobulated areas of chorioretinal atrophy

FIG. 4. Case 4. Lateral roentgenogram of skull showing areas of calcification throughout both cerebral hemispheres.

with small strips of normal retina between them. Some of this disturbance extended into the macula itself. Beginning at the lower part of the macula and extending below was a huge excavated, particularly well-circumscribed, white, atrophic area bordered with black pigment. Throughout all of these areas pigment disturbance was found. There were several areas of proliferation in the periphery."

Serum neutralization test: Blood serum contained no neutralizing antibodies for Toxoplasma. It was felt that this test material may not have been in good condition when received and thus might have accounted for the negative findings. It has not been possible to have this test repeated.

Summary: This five and one-half year old white male was noted to have difficulty in the use of his eyes when he was one year old. He had no convulsions. It was felt that he was mentally retarded. He was partially blind, with marked ocular nystagmus. He had a bilateral chorioretinitis particularly about the macular areas. The head was symmetrically enlarged and there was marked dilatation of the lateral ventricles with a dilated cyst of the septum pellucidum. Serum neutralization test was negative, but the test material was not considered satisfactory.

Case 4. G.D., a seven-month-old white, first-born male, was referred to the University Hospital by Dr. Eleanor Stein of Harrisburg, Pa. The mother and father were both living and well, although the mother was said to have had some sort of kidney disorder before the delivery of this child. A

second child was born recently and is healthy. The patient had pylorospasm and broncho-pneumonia when one month old. At four months, he had otitis media, a gastro-enteritis and repair of a congenital left inguinal hernia. At this time, it was noted that his head did not seem to be enlarging properly. His behavior was considered abnormal for his age. At times, he would roll his eyes upward. He was not able to see very well. He did not seem to be able to use his right lower extremity freely. It was held rather stiffly and occasionally tremors were seen in it. He vomited intermittently.

Examination: The patient was fairly well developed and nourished. He weighed 6.4 kg. The head was obviously microcephalic. Anterior and posterior fontanelles were closed. Head circumfer-

FIG. 5. Case 4. Drawing of right retina from Case 4. See detailed description in text.

ences was 25.5 cm., while the chest measured 41 cm. The skull was somewhat asymmetric with a flattening in the right occipital region and lack of prominence in the frontal areas. There was an irregular rolling movement of the eyeballs. His eyes did not observe light or follow moving objects. The eyeballs moved aimlessly about the orbits and usually were pulled upward and outward to either side. Pupils reacted to light. He moved all of his extremities; deep reflexes were all present; and there were no pathologic reflexes. He occasionally smiled and noxious stimuli were appropriately perceived throughout the body. On occasions, his limbs would stiffen out in a tonic spasm of momentary duration.

Laboratory studies: Blood count showed 10.9 gm. hemoglobin and 8900 leucocytes. The urine showed nothing abnormal. Cerebrospinal fluid showed protein 50 mg./100 cc. fluid, sugar 69 mg./100 cc. fluid. Attempts were made by centrifuging the cerebrospinal fluid to locate the toxoplasma, but none was found by this technic. Roentgenogram of the abdomen showed nothing abnormal. Skull roentgenogram (Fig. 4) showed small areas of calcification throughout both cerebral hemispheres. Pneumoencephalogram was attempted but only a small amount of spinal fluid could

be removed and the amount of air seen was localized around the basal cisternae. No air was present in the ventricles.

Ophthalmologic examination: This was done under ether anesthesia, and at the same time a drawing was made of the right optic fundus (Fig. 5). "In the right eye many fine strands could be seen running from the iris onto the lens surface, characteristic of an extensive persistence of the pupillary membrane. A few, fine vitreous opacities could be noted. The right optic nerve head was gray-white in color. The borders were not distinct. The nasal margin of the disc was more blurred than the temporal border. The retinal vessels seemed narrowed. There were two large patches of chorioretinitis. One was over the macular area. The other was temporal and approximately two disc diameters from the macula and slightly below it, below the midline. These lesions were irregularly ovoid. They have a pigmented border surrounding the areas of atrophy of the retina and choroid. At the base of each area of atrophy, the white sclera could be seen and occasionally a broad, deep choroidal vessel. In the left eye, the persistent pupillary membranes were not as extensive as in the right eye. There were many vitreous opacities. The optic nerve was also grayish white with blurred margins and evidence of tissue proliferation. The retinal vessels were narrowed and the large patch of chorioretinitis could be seen in the macular area, extending temporally and downward. It measured about two disc diameters in size. It was irregularly ovoid in shape, with varying depths of surrounding pigment accumulations. The white sclera could be seen through this area of atrophic retina and choroid."

Serum neutralization test: The serum was positive for Toxoplasma. A specimen of his mother's serum was sent for testing at the same time, but was technically unsatisfactory. Further specimens were not available.

Summary: This seven-month-old, white male had pylorospasm and bronchopneumonia at one month and gastro-enteritis, otitis media and repair of a left congenital inguinal hernia at four months. Microcephaly was noted at this time. He had irregular movements of his eyeballs and periodic spasms of his extremities. Bilateral optic atrophy and areas of chorioretinitis were seen. Scattered intracerebral calcifications were present. Blood serum contained neutralizing antibodies for Toxoplasma.

Case 5. B.M., a nine-month-old, white female, was admitted to the Hospital of the University of Pennsylvania on the service of Dr. Wilfred E. Fry for enucleation of the left eye for diagnostic purposes. She was a full-term infant weighing 3100 gm. at birth. At three months, the child was thought to have poor vision due to a congenital anomaly of both eyes. Microphthalmos was also noted.

This was the second child of normal, healthy parents. There were two healthy siblings. There were no family illnesses.

Examination: The patient appeared well developed and well nourished. Head appeared slightly larger than normal. It measured 45.5 cm. in circumference and the chest 42.5 cm. She was 68.5 cm. long, and showed inability to hold her head erect. It was felt that she was mentally retarded.

Laboratory studies: Skull roentgenograms showed linear calcifications in the posterior and inferior portions of the frontal lobes. No serum neutralization tests were done.

Ophthalmologic examination: "The eyeball on the right was of normal size, the iris normal with perhaps definite but sluggish response to direct stimulation. No response could be found consensually from the right to the left. Dilated normally with atropine. The disc was large and had a shallow, saucer-shaped excavation, pale and surrounded with retinal and choroidal atrophy below. Inferiorly, and in the inferior temporal region there was a large area of confluent chorioretinitis starting from the nerve head, gray-white to black with profound pigment changes in places and somewhat elevated. The left eye was definitely microphthalmic, irresponsive to direct and consensual reflexes, and the iris thick and muddy without response to moderate atropinization. The fundus here, nasally, is somewhat dissimilar to the right. There is new formed tissue in the nasal half of the fundus, going past the midline, rimmed with pigment changes."

Pathologic report on the enucleated left eye: (Dr. Abner Wolf)[1] "The retina is considerably thickened in places and projects forward irregularly into the posterior chamber. Many of the cells of the ganglionic layer have disappeared. The stratum opticum is thickened due to gliosis and in it small perivascular collections of plasma cells and lymphocytes are encountered. The molecular and nuclear layers are interrupted and displaced by bands of glial tissue in which there are varying

numbers of similar inflammatory cells, usually scanty. The dislocation of the retina into the posterior chamber and the disarrangement of the layers mentioned produces papillary protuberances in which the layering is quite obscure. There are numerous cysts of varying size in the degenerated portions of the retina and these contain pink granular material. The layer of rods and cones is well preserved in some areas and is the site of considerable gliosis in others. The pigmented layer of the retina is considerably hypertrophied in some zones and its cells extend inward into the retina. The choroid and sclera show no unusual features. No Toxoplasmata are encountered.

The presence of evidence of chronic inflammation and of considerable degeneration and gliosis of the retina are compatible with the possibility of toxoplasmic infection. The absence of any inflammation in the choroid layer and, above all, the absence of protozoa cast some doubt upon this diagnosis. It is possible, however, that an infection which is long passed may be compatible with these findings."

Summary: This nine-month-old, white female was blind from birth and had a left microphthalmos. She was unable to hold her head erect and was mentally retarded. She showed areas of chorioretinitis and optic atrophy. The head was enlarged. Left eye was enucleated and microscopic studies showed areas of chorioretinitis. Skull roentgenograms showed calcifications in the frontal regions. No serum neutralization tests were done.

Case 6. R.J., a Negro male was studied by Dr. Henry T. Wycis of Temple University Hospital and subsequently examined by one of us (G.S.).

He was the first-born. Birth was spontaneous at full-term. He weighed 2500 gm. at birth. The mother noticed that he did not seem to be aware of his environment and had a weakness of the left extremities. She also noticed that there was a squint of the eyes and felt that he was not able to see things at a distance. Objects had to be very close before he would recognize them. He seemed to do everything with his right hand and failed to use his left hand. The left foot turned inward. He developed slowly and was not able to sit up or stand alone at the usual time.

Examination: At fourteen months, the cranial contour was normal. Pupils were equal and reacted well to light. There was bilateral weakness of the sixth nerve with ocular type of nystagmus. Facial movements seemed less pronounced on the left side than on the right. There seemed to be some narrowing of the left palpebral fissure. There was weakness and spasticity of the left upper and lower extremities. Deep reflexes seemed to be increased on both sides, but more so on the left. Babinski and Hoffman signs could not be elicited. The left foot turned inward and there was some tendency to crossed-scissors gait.

Laboratory studies: Studies of the blood and urine were entirely normal. Spinal fluid showed a cell count of 18, 60% of which were leukocytes and 40% were lymphocytes. The test for syphilis on the spinal fluid was negative. Protein, sugar and chlorides were within normal limits.

Roentgenogram of the skull showed calcifications somewhat symmetrically distributed on both sides of the brain, throughout many parts of the cerebrum.

Pneumoencephalogram showed both lateral ventricles to be enlarged. Third and fourth ventricles were not visualized. There seemed to be definite evidence of rather irregular but widespread brain atrophy. Cisterna interpeduncularis was increased in size.

Ophthalmological examination: The child had a high myopia. Areas of old healed choroiditis were scattered throughout the fundi.

Serum neutralization test: The serum was positive for Toxoplasma.

This patient was again examined by one of us (G.S) when he was two years and ten months of age. Head circumference at that time was 44.5 cm. Ocular nystagmus was marked. He did not talk. He seemed to understand very well what was said to him. He was able to hold his head up well. He could not stand alone. When supported, he walked with a rather spastic gait and with a tendency to drag the left lower extremity. Movements of the upper extremities were somewhat incoordinate, although he was able to hold on to objects which were placed in his hands. He did not reach spontaneously for objects. There was a definite tendency for him to use the right upper extremity more freely than the left. Deep reflexes seemed to be hyperactive throughout, although possibly a bit more on the left side. This was particularly true of the left lower extremity. There were no pathologic reflexes.

Summary: This three-year-old, Negro male showed a weakness of the left extremities and squint of the eyes at three months. He had ocular nystagmus and areas of old healed choroiditis.

He was mentally retarded. There were scattered intracerebral calcifications and both lateral ventricles were enlarged. The serum neutralization test was positive for Toxoplasma.

Analysis of Cases

The similarity between the clinical features of these six cases and of those previously described in the literature was carefully noted. Analysis of our cases (Table I) shows the uniform presence of certain characteristics of the disease and the variable occurrence of others.

TABLE I

Analysis of Cases

	Case 1 M.S.	Case 2 T.P.	Case 3 R.N.	Case 4 G.D.	Case 5 B.M.	Case 6 R.J.
Sex	F	F	M	M	F	M
Race	W	W	W	W	W	N
Age at onset	9 weeks	uncertain	1 yr.?	4 mo.	Birth	Birth
Siblings (all well)	2	2	0	1	2	0
Signs and Symptoms						
Ocular:						
Reduced vision	+	+	+	+	+	+
Nystagmus	+	+	+	+	−	+
Chorioretinitis	+	+	+	+	+	+
Optic atrophy	+	+	+	+	+	−
Microphthalmos	−	−	−	−	+	−
Neurologic:						
Convulsions	+	+	−	+	−	−
Muscle twitch, tremors	+	+	−	+	−	−
Torticollis	+	−	−	−	−	−
Restlessness	+	−	+	−	−	−
Disturbed gait	−	−	+	−	−	+
Spastic extremities	−	−	−	+	−	+
Macrocephalus	−	−	+	−	+	−
Microcephalus	−	−	−	+	−	−
Internal Hydrocephalus	+	+	+	−	−	+
Speech difficulty	−	−	−	−	−	+
Mental retardation	+	+	+	+	+	+
Cerebral calcifications	+	+	−	+	+	+
Spinal fluid						
High protein	−	−	+	+	not exam.	−
Neutralization test	+	+	unsatis.	+	not done	+

The age at onset was most difficult to determine in our cases. We have no data to suggest whether the disease process began before or after birth. All of our patients, though retarded and blind, are alive today. Sex was evenly distributed and only one of our cases was a Negro. From a practical viewpoint, reassuring to the family, it is observed that these are isolated cases. Healthy siblings were born before and after these patients.

The ocular findings seemed to be somewhat more constant. The most characteristic ocular symptom was impairment of vision. All of our cases showed this disorder and all six likewise showed evidence of focal chorioretinitis. Ocular nystagmus was noted in five of the cases, as was optic atrophy. In one instance microphthalmos was present, for which the eye was later enucleated and studied.

TABLE II

REVIEW OF CASES REPORTED IN THE LITERATURE

Age Group	Author	Year	Total Cases Reported	Autopsy	Living
Infantile or congenital	Wolf, Cowen and Paige[2,7,8,9,11]	1937–1942	11	5	6
	Janku,[12] Richter,[13] Torres[15] and deLange[16] restudied by W., C., and P.[11,14,17]	1937–1942	4	4	
	Levin and Moore[18]	1942	1		1
	Sabin[19]	1942	1		1
	Crothers[20]	1943	10		10
	Vail, Strong and Stephenson[21]	1943	6		6
	Steiner and Kaump[22]	1944	2	2	
	Guimeraes[23]	1944	1		?
	Zuelzer[24]	1944	3	2	1
	Buchanan and Lara-Gonzales[25]	1945	8	3	?
	Dow[26]	1945	2		2
	Burke[27]	1945	1		1
	Tomlinson[28]	1945	1	1	
	Adams, Horns and Eklund[29]	1946	1		1
	Robertson[30]	1946	2		2
	Pratt-Thomas and Cannon[31]	1946	1	1	
	Callahan, Russell and Smith[32]	1946	5	5	
	Ricci[33]	1946	1		1
	Miller[34]	1947	1		1
	Robinson[35]	1947	1		1
Juvenile	Sabin[3]	1941	2	1	1
Adult	Pinkerton and Weinman[4]	1940	1	1	
	Pinkerton and Henderson[5]	1941	2	2	
	Guimeraes[23]	1944	1	1	
Probable cases	Syverton and Slavin[36]	1946	1		1
	Rucker[37]	1946	1		1
	Ryerson[38]	1947	1		1
	Binkhorst[39]	1947	1		1
Total			73	28	39+

In all but one of the cases, multiple cerebral calcifications were seen in the roentgenograms. Positive neutralization tests were obtained with the serum of four of the patients. The test was not considered satisfactory in one other case because of the condition of the serum when received at the laboratory. On the other patient, the test was not done.

Of the neurologic symptoms and signs, convulsions were present in three of the six

cases. These attacks were generalized and sporadic. Some were associated with febrile episodes. No adequate follow-up data is available at this point, but the convulsive state has not subsequently occupied a prominent role in the patients' lives. Muscle twitchings or tremors were noted in three of the cases. Torticollis (ocular) was observed in one child only. Restlessness was reported in two of the children. Disturbance of gait and spasticity of extremities were noted in two cases each. Macrocephalus was described in two of the cases while microcephalus was noted in only one patient. In four of the six cases there was evidence of internal hydrocephalus. In one of the remaining cases the pneumoencephalogram was not satisfactory and in the other case it was not done. There was mental retardation noted in all six of these cases but only in one of the children was there speech difficulty.

In our series of cases the blood studies showed no variation from the normal values for children. In two of the cases where the spinal fluid was examined, there was a high protein value.

Discussion

With the introduction of such diagnostic aids as animal inoculation and neutralization tests for antibodies, the number of reported cases of human toxoplasmosis has reached nearly 75 (Table II). The first proven case was described by Wolf, Cowen and Paige in 1939.[2] In this and succeeding papers they presented the characteristic features of infantile toxoplasmic encephalomyelitis, which was thought to be rapidly fatal. Since then, cases of toxoplasmosis have been described in older children (Sabin)[3] and in adults (Pinkerton).[4, 5] The clinical features of this infection in the various age groups differ and there may be an acute phase of the disease or a latent, chronic phase in which the clinical manifestations are chiefly the residual effects of the infection.

In the two cases reported by Sabin in older children, the clinical picture is one of acute encephalitis without the ocular lesions and other prominent features of the infantile form. This has been designated the juvenile type and seems to be acquired rather than congenital.

The clinical picture of adult toxoplasmosis may resemble typhus or Rocky Mountain spotted fever with little brain involvement. A generalized maculopapular skin eruption sparing scalp, palms and soles of the feet was observed. There were clinical and roentgenologic evidences of interstitial pneumonitis. All adult cases seemed to have been acquired and were fatal.

A number of individuals having no history of clinical toxoplasmosis were studied and the sera of many of them was found to contain neutralizing antibodies for strains of Toxoplasma (Sabin).[6] Whether these persons had recovered from an undiagnosed Toxoplasma infection or were carriers of the disease has not been determined, but it does suggest that the incidence of toxoplasmosis is probably much greater than clinical and pathologic reports have already shown.

The chief features of infantile toxoplasmic encephalomyelitis, as already described in the literature by Cowen, Wolf and Paige,[7] are: (1) onset at birth or soon after, (2) convulsions, (3) bilateral communicating hydrocephalus, (4) bilateral focal chorioretinitis usually involving both macula and (5) multiple calcifications of the brain. In children who survive this acute stage the picture becomes more modified. It is in this phase that the differential diagnosis is important.

Ophthalmologic findings: Clinical: Reduction of vision is one of the most disturbing factors to the patient with latent toxoplasmosis. Bilateral focal chorioretinitis involving both macula, as a rule, was severe and extensive.[9] These lesions were frequently multiple

and when observed were quiescent or healed. They consist of areas of exposed choroid which are surrounded and covered by a varying amount of pigment. In the quiescent stage, the vitreous is clear. The retina and its vasculature intervening between the lesions was apparently normal. Microphthalmos was occasionally observed.

Pathologic: For purposes of comparison with our own case, the histopathologic observations made by Koch, Wolf, Cowen and Paige[9] on the eyes of three of their patients are of interest. They noted focal areas of congestion and edema involving all the layers of the retina, but especially the inner three layers. Necrosis of all the lamina occurred in the central portion of the lesions but, at times, only the inner layer showed degeneration. Normal structures were seen to be replaced by amorphous cystoplasmic and nuclear debris. Perivascular and diffuse infiltration by lymphocytes, plasma cells and occasionally eosinophiles and lipoid-laden phagocytes were present, chiefly at the margins of the necrotic areas. Polymorphonuclear leukocytes were observed at times. Small amounts of exudate could be seen on the free surface of the internal limiting membrane and were often associated with ingrowth of fibroblasts and capillaries into the vitreous. At the margins of the necrotic zones the retinal architecture was considerably distorted. The choroid was moderately infiltrated in areas near the retinal lesions. The choriocapillary layer was congested and infiltrated by plasma cells, lymphocytes and eosinophiles. A less dense cellular exudate and edema were present in some parts of the lamina vasculosa. The sclera was normal. The leptomeningeal sheaths of the optic nerve were mildly infiltrated by cells similar to those seen in the choroid.

In a differential diagnosis of ocular disorders, the clinical signs and symptoms are a valuable adjunct when ophthalmoscopic observations are not conclusive. Involvement of the nervous system, convulsions, cerebral calcifications, serologic tests and duration and course of the illness must all be considered. Ophthalmoscopically, toxoplasmic chorioretinitis must be differentiated from a number of conditions. Pseudoglioma may be difficult to distinguish from an old chorioretinitis but is usually single and unilateral. In addition, the anterior segment of the eye usually shows signs of previous inflammation. Retinoblastomas may be recognized by the yellowish reflex at the pupil and elevated intraocular tension. Gliomas may be bilateral and progress from a small nodule to a large polypoid mass protruding into the vitreous. Traumatic sequelae produce scars which are unilateral and single. The single macular lesion of cerebromacular degeneration differs in appearance from the multiple lesions of toxoplasmic chorioretinitis. Congenital developmental defects such as colobomas of the choroid, optic disc, retina and macula do not typically appear in the upper half of the fundus and are easily distinguished from the lesions of toxoplasmosis. The ocular lesions of tuberous sclerosis differ so markedly from toxoplamic chorioretinitis that they are not easily confused. Acute metastatic chorioretinitis, associated with the acute exanthemata and other protozoan diseases, occurs after the disease has been well established. The lesions occur rapidly and metastatically, are small and irregulr but widely distributed throughout the fundus. Generalized uveal infection frequently occurs. In retrolental fibroplasia the pathology is immediately behind the lens.

In ocular syphilis the characteristic lesions are small, diffuse and regular in distribution on the fundus. The choroidal lesions of tuberculosis are small, dull yellow focal areas distributed irregularly in the choroid. In a differential diagnosis of any of these, the clinical picture as a whole must be carefully considered.

Roentgenologic features: Two of the most important diagnostic features of toxoplasmic encephalomyelitis are revealed by roentgenology (Dyke et al.).[8] Cerebral calcifications

and internal hydrocephalus are among the most constant findings in this condition. The calcified lesions averaged from 1-3mm. in diameter and occurred primarily in the cortex of all the cerebral lobes and in the basal ganglia and thalami. In the two latter, the calcium deposits occasionally appear as curvilinear streaks.

Skull enlargement, bulging of the fontanelles, separation of the sutures and dilated ventricles, as seen in the pneumoencephalogram, indicate internal hydrocephalus.

Cases of toxoplasmic encephalomyelitis in this latent or inactive stage may often be misdiagnosed and must be differentiated from other conditions such as congenital malformations or tumors of the brain, birth injury, tuberous sclerosis and cerebromacular degeneration. The skull roentgenograms are valuable adjuncts in the differential diagnosis of intracranial lesions which may undergo calcification. In brain tumors, which are more common in older children than in infants, the calcification is focal and limited to a single area.[8] The craniopharyngioma is characterized by calcification in and above the sella turcica. The venous angioma may show calcium deposits in linear streaks which are often parallel. In tuberous sclerosis the calcifications are usually situated along the roofs of the lateral ventricles, though they may be found in the lateral part of the cerebral hemispheres.

"Cerebral calcification epilepsy" and "symmetrical cerebral calcification" have been described as occurring in older children and adults. Calcified subdural hematoma shows calcium deposits adjacent to the inner table of the skull and in the form of linear streaks, as well as punctate forms.

Tuberculoma, a rare lesion of infants and children, usually shows localized lesions in the region of the cerebellum when calcifications occur. Cysticercus cellulosae, though rare, may occur in adults. The calcifications are along the posterior limb of the Sylvian fissure and the base of the brain, not involving the deeper portions.

Clinical neurologic considerations: In the infantile form of toxoplasmosis the tissues of the central nervous system appear to be particularly susceptible to invasion and injury by the protozoan. When the child survives the acute phase, the clinical neurologic picture is one resulting from inflammation and focal necrosis of the brain and meninges. Healing of these lesions takes place with the formation of areas of calcification. The characteristic neurologic features consist of convulsions, evidence of internal hydrocephalus, mental retardation and often speech difficulty.[7] The retina is involved by focal destructive lesions and evidence is seen of healed chorioretinitis. Other ocular disorders, such as nystagmus and strabismus, are frequently present and will be mentioned later. Because of the widespread distribution of the lesions in the central nervous system, the neurologic signs and symptoms are variable. Irritability and hyperactivity are not unusual. Microcephalus has been noted in a few cases. Twitching and tremors of the extremities may be evident. Deep reflexes may occasionally be hyperactive.

Clinical laboratory studies: Studies of the spinal fluid from cases reported in the literature showed varying results. An increase in the protein content of the fluid was frequently noted. Pleocytosis occurred on occasion with lymphocytes predominating. Toxoplasma have been isolated from the spinal fluid in cases diagnosed as toxoplasmosis (Miller and Ryerson).[34, 38]

Blood studies do not show much variation from the normal values, except for an occasional leukopenia or anemia. Serum neutralization tests showed the presence of antibodies to Toxoplasma in a large percentage of the cases tested by Cowen[7] and others.

Despite the establishment of a fairly well-defined picture of toxoplasmic encephalomyelitis, there are many gaps in our knowledge of the disease. The problem of transmission

of the infection and animal vectors is still unsolved. The possibility of human carriers of the infection has been suggested. Because positive serum reactions have been obtained in a number of persons[6] showing no clinical symptoms or signs of the disease whatever, the value of serum neutralization tests as a diagnostic aid has been questioned. The existence of a subclinical or chronic state of toxoplasmosis has been postulated. However, the clinical picture, even without the serum neutralization tests and identification of Toxoplasma in body fluids, seems sufficiently well-defined to make the diagnosis on these grounds alone. Though the diagnosis may be made clinically at an early age, there is still no effective means of prevention or therapy. Recent experiments with sulfapyridine by Weinman and Berne[10] have been more or less promising but much work remains to be done in this field. In the meantime, it is the concern of the neurologist, pediatrician, ophthalmologist, pathologist and general practitioner to be on the alert to recognize the disease and to record any observation which will aid in the knowledge and prevention of the infection. Since there is little to be expected from therapy, once the irrevocable changes in the brain and retina have taken place, the prevention of the disease is the challenging factor in future studies of toxoplasmic encephalomyelitis.

Summary

Six cases of toxoplasmic encephalomyelitis in infants and children are presented. In all of these cases, the diagnosis was made on clinical grounds alone. All of these patients are still living. A description of the pathologic findings in the retina of one case is given.

In an analysis of these six cases it was noted that the ocular findings were the most constantly occurring of all the features. Mental retardation was also noted in all six cases. Cerebral calcifications were found in all but one of the cases.

The cases already reported in the literature are enumerated and a review of the clinical features of toxoplasmic encephalomyelitis is given. The chief features noted in the infantile form are: (1) onset at birth or soon after, (2) convulsions, (3) bilateral communicating hydrocephalus, (4) bilateral focal chorioretinitis usually involving both macula and (5) multiple calcifications in the brain.

It is our feeling that this constellation of signs and symptoms should suggest the diagnosis of toxoplasmosis without recourse to the isolation of the protozoan or the securing of positive neutralization reactions.

Acknowledgment

The authors wish to express their sincere gratitude to Dr. Abner Wolf and his associates at Columbia University College of Physicians and Surgeons for so graciously performing the neutralization tests for Toxoplasma on the sera of our patients and for the microscopic examination of the retina of our fifth case.

References

1. Wolf, Abner, Personal communication.
2. Wolf, A., Cowen, D., and Paige, B. H., Toxoplasmic encephalomyelitis; new case of granulomatous encephalomyelitis due to a protozoan, Am. J. Path 15:657, 1939.
3. Sabin, A. B., Toxoplasmic encephalitis in children, J.A.M.A. 116:801, 1941.
4. Pinkerton, H., and Weinman, D., Toxoplasmic infection in man, Arch Path. 30:374, 1940.
5. Pinkerton, H. and Henderson, R. G., Adult toxoplasmosis, previously unrecognized disease entity simulating the typhus-spotted fever group, J.A.M.A. 116:807, 1941.

6. Sabin, A. B., Toxoplasma neutralizing antibody in human beings and morbid conditions associated with it, Proc. Soc. Exper. Biol. & Med. **51**:6, 1942.
7. Cowen, D., Wolf, A., and Paige, B. H., Toxoplasmic encephalomyelitis; clinical diagnosis of infantile or congenital toxoplasmosis; survival beyond infancy, Arch. Neurol. & Psychiat. **48**:689, 1942.
8. Dyke, C. G., Wolf, A., Cowen, D., Paige, B. H., and Caffey, J., Toxoplasmic encephalomyelitis; significance of roentgenographic findings in diagnosis of infantile or congenital toxoplasmosis, Am. J. Roentgenol. **47**:830, 1942.
9. Koch, F. L. P., Wolf, A., Cowen, D., and Paige, B. H., Toxoplasmic encephalomyelitis; significance of ocular lesions in diagnosis of infantile or congenital toxoplasmosis, Arch. Ophth. **29**:1, 1943.
10. Weinman, D., and Berne, R., Therapeutic cure of acute experimental toxoplasmosis in animals, J.A.M.A. **124**:6, 1944.
11. Wolf, A., and Cowen, D. Granulomatous encephalomyelitis due to encephalitozoan (encephalitozoic encephalomyelitis), Bull. Neurol. Inst. New York **6**:306, 1937.
12. Janku, J., Parasites in coloboma of macula, Cas.lek.cesk. **62**:1021, 1923.
13. Richter, R., Meningo-encephalomyelitis neonatorum; anatomic report, Arch. Neurol & Psychiat. **36**:1085, 1936.
14. Wolf, A., and Cowen, D., Granulomatous encephalomyelitis due to protozoan (toxoplasma or encephalitozoan); identification of case from literature, Bull. Neurol. Inst. New York **7**:266, 1938.
15. Torres, C., Affinités de l'encephalitozoan chagasi, agent étiologique d'une meningo-encéphalomyélite congénitale avec myocardite et myosite chez l'homme, Compt. rend. Sec. de Biol. **97**:1797, 1927.
16. deLange, C., Klinische und pathologisch-anatomische Mitteilungen über Hydrocephalus chronicus congenitus und acquisitus, Ztschr. f.d. ges. Neurol. u. Psychiat. **120**:433, 1929.
17. Paige, B. H., Cowen, D., and Wolf A., Toxoplasmic encephalomyelitis; further observations of infantile toxoplasmosis; intrauterine inception of the disease; visceral manifestations, Am. J. Dis. Child. **63**:474, 1942.
18. Levin, P. M., and Moore, H., Fetal toxoplasmic encephalitis—type of congenital cerebral disease, J. Pediat. **21**:673, 1942.
19. Sabin, A. in deSanctis, A. G., Advances in Pediatrics Vol. 1,, Interscience Publishers, New York, 1942.
20. Crothers, B., Toxoplasmic encephalitis: clinical experience, Arch. Neurol & Psychiat. **49**:315, 1943.
21. Vail, D., Strong, J. C., Jr., and Stephenson, W. V., Chorioretinitis associated with positive serologic tests for toxoplasma in older children and adults, Am. J. Ophth. **26**:133, 1943.
22. Steiner, G., and Kaump, D. H., Infantile toxoplasmic encephalitis, J. Neuropath. & Exper. Neurol. **3**:36, 1944.
23. Guimaraes, F. N., Toxoplasmic encephalitis, J.A.M.A. **124**:252, 1944.
24. Zuelzer, W. W., Infantile toxoplasmosis; with report of three new cases, including two in which patients were identical twins, Arch. Path. **38**:1, 1944.
25. Buchanan, D., and Lara-Gonzales, C., Clinical pathologic and experimental study, Arch. Neurol. & Psychiat. **53**:447, 1945.
26. Dow, R. S., Toxoplasmic encephalitis, Northwest Med. **44**:382, 1945.
27. Burke, F., Toxoplasmosis, Clin. Proc. Child. Hosp. **1**:125, 1945.
28. Tomlinson, W. J., Human chronic toxoplasmosis, Am. J. Clin. Path. **15**:123, 1945.
29. Adams, F. H., Horns, R., and Eklund, C., Toxoplasmosis in large Minnesota family, J. Pediat. **28**:165, 1946.
30. Robertson, E. G., Toxoplasmic encephalomyelitis, J. Australia **2**:449, 1946.
31. Pratt-Thomas, H. R., and Cannon, W. M., Systemic infantile toxoplasmosis, Am. J. Path. **22**:779, 1946.
32. Callahan, W. P., Russell, W. O., and Smith, M., Human toxoplasmosis, Medicine **25**:343, 1946.
33. Ricci, H. N., Congenital toxoplasmosis, Am. J. Ophth. **29**:1590, 1946.
34. Miller, M. C., Infantile toxoplasmosis, J. Pediat. **30**:201, 1947.

35. Robinson, P., Case of toxoplasmosis with recovery, Ann. paediat. **168**:134, 1947.
36. Syverton, J. T., and Slavin, H. B., Human toxoplasmosis, J.A.M.A. **131**:957, 1946.
37. Rucker, C. W., Seesaw nystagmus associated with choroiditis and positive neutralization test for toxoplasma, Arch. Ophth. **35**:301, 1946.
38. Ryerson, F. S., Probable toxoplasmal chorioretinitis, Am. J. Ophth. **30**:212, 1947.
39. Binkhorst, C. D., Toxoplasmosis; parasitologically demonstrated diagnosis (?); Significance of clinical manifestations of infantile toxoplasmosis, Maandschr. v. Kindergeneesk **15**:1, 1947.

SPANISH ABSTRACT

Encefalomielitis Toxoplasmosica

Seis casos de encefalomielitis por toxoplasma son presentados en este trabajo. En todos estos casos el diagnostico fue hecho solamente en el terreno clinico. Todos los pacientes viven aun. Una detallada descripcion de los hallazgos patologicos observados en la retina de uno de estos casos es considerada especialmente.

En el analisis de los seis casos puede comprobarse que las lesiones oculares ocurren con una mayor constancia quelos otros hechos clinicos. El retardo mental tambien estuvo presente en los seis casos y calcificaciones cerebrales fueron observadas en cinco de ellos.

Los casos reportados hasta el presente en la literatura medica, son enumerados y revisados desde el punto de vista clinico en lo que a la encefalomielitis toxoplasmica se refiere.

Los principales hechos notados en la forma infantil de esta afeccion son: 1.—Comienzo desde el nacimiento o inmediatamente despues. 2.—Convulsiones, 3.—Existencia de hidrocefalia bilateral comunicante. 4.—Coriorretinitis bilateral focal afectando ambas maculas. 5.—Multiples calcificaciones cerebrales.

El criterio de los autores es que este conjunto de signos y sintomas debe hacer pensar en el diagnostico de toxoplasmosis aun cuando no se aislen el protozoario o se recurra a la reaccion positiva de neutralizacion.

255 S. 17th St.

SALICYLATE TOLERANCE AND TOXICITY IN CHILDREN

By EMANUEL DUBOW, M.D., AND NATHANIEL H. SOLOMON, M.D.
New York, N.Y.

INTRODUCTION

SALICYLATES are one of the common drugs administered to children. They have long been used to alleviate symptoms in rheumatic fever, and the recent work of Coburn[1] has revived interest in their use as a therapeutic agent in this disease. Using dosage of sodium salicylate from 0.13 to 0.19 gm./kg. body weight daily in young adults for prolonged periods, he reported there was no instance of salicylate toxicity. Since a standard textbook states,[2] "children are quite tolerant of salicylates and require larger doses than calculated by their age and weight," a similar experience with children might be expected. That such was not the case was indicated when Stevens and Kaplan[3] administered the same relative dosage of sodium salicylate (0.15 gm./kg.) to patients acutely ill with rheumatic fever and reported three cases of salicylate intoxication including one death. On the other hand Fashena and Walker[4] administered a similar dosage (0.15 gm./kg.) to convalescent patients and noted no toxicity for periods up to nine days. With larger dosage (0.2 to 0.22 gm./kg.) they noted signs of salicylate intoxication after a short time. Other investigators[5, 6, 7] have reported conflicting results.

In view of the difference of opinion regarding the incidence of toxicity and the dosage at which the toxicity manifests itself, this study was undertaken.

The ingestion of salicylate is followed rapidly by absorption, general distribution and excretion as demonstrated by Hanzlik.[10] Eighty percent appears eventually in the urine as salicyl compounds and 20% as breakdown products. Since excretion is rapid, a time schedule of dosage must be used. When salicylate is given every four hours over long periods of time cumulative effects may be noted.[4, 5, 11] It has been shown[11, 12, 13] that early in the administration of large doses of salicylate there is a decrease of serum CO_2 content. This has been attributed to a "blowing off" effect due to stimulation of the centers in the central nervous system by salicyl compounds. Hyperpnea and the low CO_2 content should not be interpreted as manifestations of acidosis. The loss of CO_2 content with consequent decrease of bicarbonate leaves a transient predominance of fixed base, and an alkalosis manifested by an elevation of pH values. Later there is some compensation by increase in serum chlorides. Moreover if large doses of salicylate are continued and CO_2 levels remain low, a gradual loss of base through the urine occurs so that true acidosis develops. In acute infections accompanied by fever, anorexia, and dehydration, the tendency toward acidosis is enhanced. In the presence of high tissue salicylate levels, increased muscle lactate and acid metabolites[13] all combine to produce an acidosis.

Quincke[8] in 1882 noted hyperpnea and described it as "salicyl dyspnea." He observed that prolonged use of sodium salicylate might be followed by increased respiration. Hyperpnea appeared early and characteristically was deep, pauseless, and closely resembled the hyperpnea of diabetic acidosis. The rate of respiration or the depth, or both, may increase, but there was no decrease, although a normal rate with increased depth might

From the Pediatric Service of Dr. Philip Cohen, Beth Israel Hospital, New York City. This work was aided by funds from the Loyal League Philanthropies Inc., New York, N.Y.
(Received for publication January 8, 1948.)

give the impression of decreased rate. Also it has been shown[9] that vomiting is central in origin rather than a result of gastric irritation.

Urinary findings in salicylate toxicity have been reviewed by Dodd et al.[14] They found that there may be reduction of copper by salicylate compounds. A purple color appears, when ferric chloride is added to the urine, which persists on boiling (Gerhardt's test). Acetone as well as diacetic acid may be present. The appearance of albumin, casts, and red and white blood cells in the urine may be evidence of kidney damage.

Increase in prothrombin clotting time[15, 16, 17] and serum chloride level[11] occur, and have been described previously.

Clinical Study

A group of 19 children were treated with varying dosage of sodium salicylate or acetylsalicylic acid and observed for signs and symptoms of toxicity. These children (Table 1) ranged in age from 8 months to 11½ years. We attempted to select cases in which salicylate therapy was indicated, and in which there was no complicating metabolic disturbance. Eleven were cases of active rheumatic fever, and all but one case (Case 2, J. S.) were acutely ill.

Blood plasma salicylate levels,[18] serum CO_2 content (standard Peters & Van Slyke procedure[19]), and pH values (by the glass electrode method, using a Leeds and Northrup potentiometer) were studied on alternate days and more frequently when deemed necessary. Routine urines, including Gerhardt and Rothera tests were performed daily.

Both sodium salicylate and acetylsalicylic acid were given without alkali in all cases. Where vomiting occurred, the drug was given in milk. Dosage was calculated by weight as either 0.10 gm., 0.125 gm. or 0.15 gm./kg. body weight, and was then divided into four doses administered at four hourly intervals during the day. The molecular weight of acetylsalicylic acid is about 180, as compared to a molecular weight of 148 for sodium salicylate. Therefore, one should be cognizant that there is only about 80% as much salicylate in acetylsalicylic acid as there is in sodium salicylate, when equal weights are taken.

Results

We attempted first to give the same dosage recommended by Coburn. Six patients between the ages of 3 and 11½ years were given salicylate 0.15 gm./kg. daily. Three of these were given two separate courses, one of sodium salicylate and one of acetylsalicylic acid, two were given sodium salicylate alone, and one was given acetylsalicylic acid alone. Five of these six developed definite toxic symptoms manifested by the following:

1. Hyperpnea was the usual presenting sign in all of the five cases that manifested toxicity. It could be overlooked easily unless looked for specifically. This is especially true because the patients were comfortable and were not conscious of any shortness of breath. A few patients who did not develop subsequent toxic effects showed a transient mild hyperpnea lasting only a few hours. In patients with active rheumatic fever undergoing salicylate therapy, it is important not to confuse hyperpnea with dyspnea due to carditis with failure.

2. Apathy and lassitude were noted in all of the five cases. Often this was very striking. The patient stared ahead blankly and showed little interest in toys or companions. Questions were answered slowly. Some patients appeared to resent being disturbed and seldom smiled.

3. An early sign of salicylate intoxication was anorexia. Three of five cases manifesting

TABLE I

Case No.	Age in Years	Weight kg.	Diagnosis	Drug§	Dose in gm./kg.	Final Plasma Levels†			Days‡
						CO_2	pH	Salicylate	
1. E.V.	11	35	Rheumatic fever	ASA	0.150*	15.7	7.28	38.9	4
				ASA	0.10	26.8	7.35	19.5	13
				ASA	0.125	21.6	7.35	35.0	16
2. J.S.	6	20	Lobar pneumonia, convalescent	SS	0.150	20.2	7.42	26.3	12
3. A.S.	8½	36	Rheumatic fever	ASA	0.150*	16.7	7.38	41.4	5
				SS	0.150*	16.9	7.35	41.1	6
				SS	0.10	22.1	7.39	21.4	9
4. E.S.	4	17	Rheumatic fever	SS	0.150*	13.0	7.30	39.1	10
5. S.A.	9½	35	Rheumatic fever	ASA	0.150*	19.2	7.39	38.3	7
				SS	0.150*	20.3	7.38	38.3	4
6. D.C.	10	25	Rheumatic fever	SS	0.150	21.4	7.40	37.4	24
				ASA	0.150*	19.3	7.30	32.3	7
7. M.R.	11	60	Rheumatic fever	SS	0.075*	18.5	7.48	32.9	6
				ASA	0.075*	14.7	7.40	21.4	4
8. F.A.	3	15	Follicular tonsillitis	SS	0.125	26.6	—	18.6	7
9. D.C.	2½	12	Cervical adenitis	SS	0.125	21.2	—	25.1	14
10. R.E.	2	12	Follicular tonsillitis	SS	0.125	21.9	—	12.5	9
11. W.V.	¾	9	Tracheobronchitis	ASA	0.150	15.1	—	17.1	3
12. M.M.	4	17	Infectious mononuc.	SS	0.150	17.2	—	27.7	5
13. L.R.	¾	9	Respiratory infection	SS	0.150	22.6	—	10.6	7
14. D.A.	10	27	Rheumatic fever	SS	0.125	22.5	7.34	35.2	20
15. M.E.	11½	35	Rheumatic fever	SS	0.125	19.4	7.32	38.9	28
				SS	0.125	21.0	7.28	37.7	20
16. E.L.	9	33	Rheumatic fever	ASA	0.125	18.9	7.38	32.6	14
17. L.H.	11	32	Rheumatic fever	SS	0.10	23.6	7.33	21.4	12
						20.2	7.31	39.4	28
18. C.R.	10½	42	Infectious mononuc.	SS	0.125	19.6	7.30	30.9	6
19. T.S.‖	9½	35	Rheumatic fever	SS	0.125*	14.9	7.26	55.1	5

* Toxicity.
† CO_2 is given as mEq./l.
Salicylates are given as mg./100 cc.
Mean values before salicylate therapy were pH 7.46; CO_2 23.2 mEq./l.
‡ Duration of salicylate therapy in days.
§ ASA—Acetylsalicylic Acid.
SS —Sodium Salicylate.
‖ Expired.

toxicity had anorexia. Nurses volunteered the information that the patient "scarcely ate anything." As toxicity increased, vomiting occurred.

4. Tinnitus was noted in two of the toxic cases in this series. Some of the older patients stated voluntarily that they had "funny noises in their ears." In others it could

be elicited by careful questioning. Tinnitus occurred early and, like hypernea, may be transient.

Other symptoms and signs of salicylate intoxication include dizziness, irritability, restlessness, disorientation, stupor, convulsions, thirst, sweating, moderate or high fever, abdominal pains, pallor, cyanosis, epistaxis, hemorrhagic phenomena and dehydration.

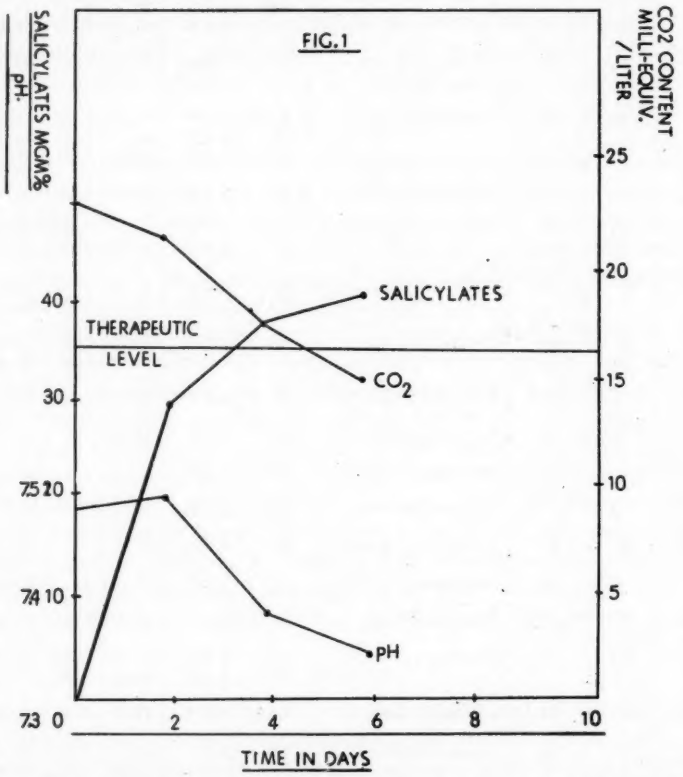


FIG. 1. Variation in salicylate, CO_2 and pH values in a group of six cases given 0.150 gm./kg. of salicylates. (Cases 1 to 6 inclusive.) Values shown are mean values for the six cases. All but one became toxic. Mean values before salicylates were pH 7.46, and CO_2 23.2 mEq./1.

In this study the administration of salicylate was stopped before the advent of these symptoms.

Plasma salicylate ranged from approximately 32 to 41 mg./100 cc. blood. Case 2, J. S., who developed no toxicity with 0.15 gm. sodium salicylate per kg. was not acutely ill, was afebrile and convalescent when salicylate was begun. All other patients with acute infections receiving this dosage of salicylate manifested toxic signs. One of them, Case 6, D. C., became toxic rapidly with acetylsalicylic acid but was able to take an equivalent dosage of sodium salicylate for 24 days without toxic effects. When acetylsalicylic acid was readministered, toxic symptoms appeared in seven days. The comparative toxicity

of sodium salicylate and acetylsalicylic acid was studied also in Case 7, M. R., who was overweight (60 kg.). We administered the calculated dosage to this patient but nausea and tinnitus developed after only two doses. The dosage was calculated then on the basis of an average weight for this age and the final value administered amounted to 0.075 gm./kg. Toxicity appeared after six days when the plasma salicylate level was 32.9

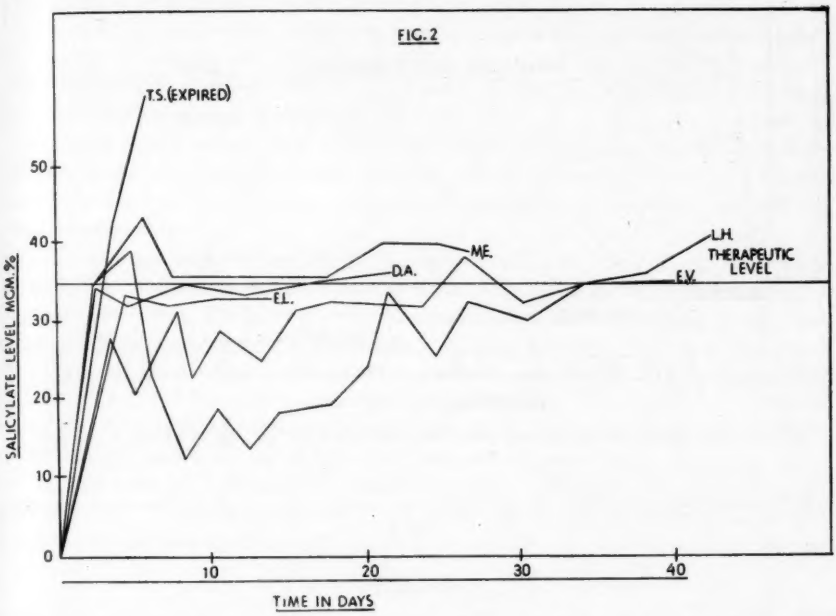


FIG. 2. Salicylate levels with dosage 0.125 gm./kg. L.H. was given 0.10 gm./kg. of salicylates until the 14th day, and was then increased to 0.125 gm./kg. E.V. was first given 0.150 gm./kg., and developed toxic signs on the 4th day. Dosage was then reduced to 0.10 gm./kg. until the 23rd day, then increased to 0.125 gm./kg. This explains the delay shown by both of these cases in achieving a therapeutic level.

mg./100 cc. blood; with acetylsalicylic acid, it appeared after four days when the level was 21.4 mg./100 cc. blood.

After observations demonstrated that toxicity appeared in the majority of patients receiving 0.15 gm./kg., the dosage was reduced to 0.10 gm./kg. However, administration of this latter dose to three cases gave plasma salicylate levels ranging from approximately 19 to 21 mg./100 cc. blood, which is considerably below the therapeutic levels (35 mg./100 cc.) advocated by Coburn.

We then administered the intermediate dosage of 0.125 gm./kg. to seven children. Levels ranging from 30.9 to 39.4 mg./100 cc. blood (Figure 2) were obtained in six patients without toxic symptoms and with normal serum CO_2 content and pH values. Case 1, E. V., who received 0.10, 0.125 and 0.150 gm./kg., demonstrates well the plasma salicylate levels obtained with each. (Figure 3.) The seventh case, T. S., with rheumatic carditis of long duration, admitted for a recurrent attack, expired suddenly on the fifth

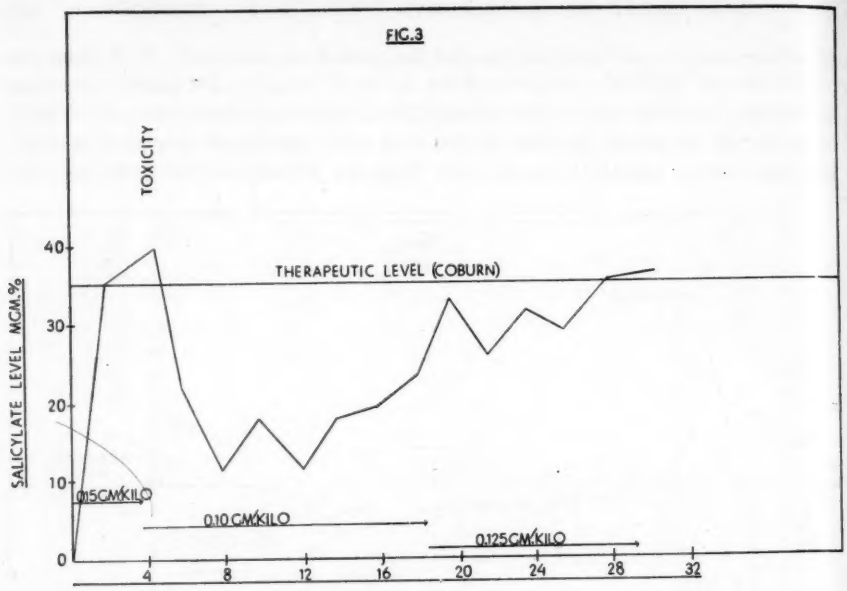


FIG. 3. E.V., age 11, given successively 0.150, 0.10 and 0.125 gm./kg. of acetylsalicylic acid.

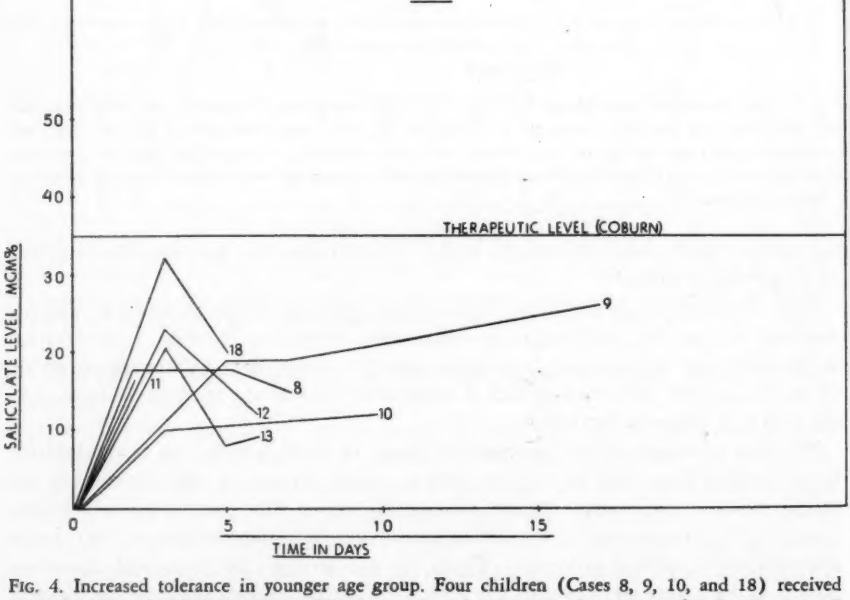


FIG. 4. Increased tolerance in younger age group. Four children (Cases 8, 9, 10, and 18) received 0.125 gm./kg. of salicylates. Three (Cases 11, 12, and 13) received 0.150 gm./kg. Levels are well below those obtained in older children.

day after admission, due to pulmonary infarction. A salicylate level obtained on the last day of life was 55.1 mg./100 cc. It may be assumed that the deranged body functions in this terminal period was responsible for the abnormally high salicylate retention.

In the patients who developed toxicity we found an early drop in serum CO_2 content, which continued to fall gradually. (Fig. 1.) When dosage was properly adjusted, the CO_2 content remained at normal levels (Table 1). The blood pH rose at first (Fig. 1), later tending to fall gradually when dosages approached the toxic levels. In some instances when full toxicity developed, the CO_2 content fell to the vicinity of 11-16 mEq./1 and pH values fell to 7.25. (Table 1.) When dosage was 0.125 gm./kg. or lower, there was little deviation from the normal in either pH or CO_2 values.

We noted in this investigation, too, the presence in various cases, largely where high salicylate levels prevailed, of albumin, casts, red and white blood cells and acetone in the urine. The Gerhardt test was positive constantly. Reduction of Benedict's solution was noted occasionally.

In two younger patients, Case 11, W. V., eight months and Case 8, F. A., three years, the dosage we had been using in the older patients succeeded in giving us only moderately high salicylate levels. Therefore a group of seven younger children ranging in age from eight months to three years were given sodium salicylate 0.125 gm./kg. (four cases) and 0.150 gm./kg. (three cases). Plasma levels obtained ranged from 10.6 to 25 mg./100 cc. blood. (Fig. 4.) None of these patients showed toxicity.

In order to serve as a base for evaluation of the figures presented, plasma pH and CO_2 determinations were made on all patients before salicylate was begun. The mean values for 19 cases were pH 7.46 and CO_2 content 23.2 mEq./1. This pH value is at the upper limit and the CO_2 content at the lower limit of the usually accepted normal values (pH 7.3-7.45; CO_2 content 23-28 mEq./1.

Comment

The investigation serves to demonstrate that dosage of the magnitude of that given to young adults by Colburn is not feasible for administration to children, for while good blood salicylate levels are obtained, toxicity occurred in five of the six children given this dosage. Lower dosage such as 0.10 gm./kg. gave blood levels which were considerably below the ranges demanded by the present trend in therapy. The optimum dosage appeared to be 0.125 gm./kg., with which dosage, satifactory levels were obtained and toxicity did not appear in seven cases.

We desire to stress the importance of hyperpnea, anorexia, apathy and lassitude as early symptoms of salicylate intoxication. In the absence of laboratory facilities to measure blood levels of salicylate, the appearance of these symptoms warrants immediate discontinuance of salicylate therapy, or marked reduction of dosage.

When massive salicylate therapy is administered and laboratory facilities are available, plasma salicylate levels, CO_2 content and pH determinations should be made. The last holds the key to proper therapy of salicylate intoxication. Low CO_2 content values do not necessarily indicate the administration of alkali. CO_2 may have been blown off during salicyl initiated hyperpnea and pH actually may be rising. Indiscriminate administration of alkali at this time might push a harmless and transitory alkalosis to dangerous levels. Fluids alone, orally and parenterally would seem to be indicated in an effort to increase renal excretion of the drug.

When both CO_2 content and pH values are low, however, the situation is dangerous,

since true acidosis is the concomitant of the severe and fatal toxicities. Here alkali is specific and should be administered freely, both orally and parenterally, until pH and CO_2 values are once again normal.

Salicylate appears to be more poorly tolerated by acutely ill than by mildly ill or convalescent children, and here other considerations come into play. Dehydration of fever and vomiting, and appearance of acid metabolites related to this condition foster the onset of a rapid and fulminating acidosis. When physiologic function is markedly deranged, as occurred in our fatal case, all of the usual rules governing salicylate administration must be set aside as even small doses may result in very high blood levels. Since 4/5 of salicylate ingested is excreted with very little change through the kidney, good function of this organ appears to be the prime governing factor in avoidance of salicylate retention. In our fatal case, terminal renal failure would be a plausible explanation for the high salicylate levels. Coincident with this investigation, we treated a case of accidental salicylate ingestion in a two year old boy who had consumed an unknown number of "aspirin" tablets. When seen first, four hours later, he showed mild pallor and hyperpnea. During the ensuing day, he voided scantily and on the following day signs of salicylate intoxication (pallor, apathy and hyperpnea) were more pronounced. Plasma salicylate determined 14 hours after ingestion was 30.6 mg./100 cc. blood and serum CO_2 content 13.4 mEq./1. However, on the next day, after large amounts of oral glucose, water, and 1/6 molar sodium lactate, he voided well, plasma salicylate fell to 7 mg./100 cc. blood and CO_2 content rose to 25 mEq./1. In this case the high salicylate level was undoubtedly related to the oliguria of the first 24 hours and may have been due in part to a direct nephrotoxic action of salicylates. In a recent report on a fatal case of salicylate poisoning, Krasnoff and Bernstein[20] demonstrated pathologic changes in the kidney. In dealing with toxicity of a drug which is largely excreted through the kidney and which may cause renal damage, support and maintenance of good renal function is a primary consideration.

In the few instances in which we were able to compare the relative toxicity of equal dosage of acetylasalicylic acid and sodium salicylate, it was our impression that the former is the more toxic drug, especially in view of the fact that acetylsalicylic acid in equal weight provides only 4/5 as much effective salicylate as the latter.

Using sodium salicylate dosage of 0.125 and 0.150 gm./kg. we failed to obtain good plasma salicylate values in patients below the age of three years. The reason may be either decreased absorption or increased excretion of salicylate. Further investigation of this point seems indicated.

Summary

1. Twenty patients were given varying dosage of salicylate with the following results:

A. Dosage of 0.15 gm./kg. daily resulted in salicylate intoxication in the majority of patients between 4 and 11 years of age.

B. Dosage of 0.10 gm./kg. failed to attain what is generally considered to be optimal therapeutic blood salicylate levels.

C. With sodium salicylate dosage of 0.125 gm./kg., therapeutic blood levels of salicylate could be maintained for long periods of time without salicylate intoxication.

2. Acetylsalicylic acid appeared to be more toxic than sodium salicylate especially since, in equal weights, it supplies only 4/5 as much salicylate as sodium salicylate does.

3. Infants and children under three years of age failed to develop therapeutic plasma levels with dosage of sodium salicylate up to 0.15 gm./kg.

4. Hyperpnea, anorexia, apathy and lassitude are the important early signs of salicylate intoxication in children.

5. Blood pH values should be a determining factor in deciding whether alkali is to be administered therapeutically in salicylate poisoning.

6. Infectious diseases, dehydration and impaired renal function are important considerations in the production and treatment of salicylate intoxication.

References

1. Coburn, A. F., Salicylate therapy in rheumatic fever, Bull. Johns Hopkins Hosp. **73**:435, 1943.
2. Goodman, L., and Gilman, A., Pharmacological Basis of Therapeutics, The Macmillan Co., New York, 1941, p. 231.
3. Stevens, D. L., and Kaplan, D. B., Salicylate intoxication in children, Am. J. Dis. Child. **70**:331, 1945.
4. Fashena, G. J., and Walker J. N., Salicylate intoxication; effects on prothrombin time and alkali reserve, Am. J. Dis. Child. **68**:369, 1944.
5. Erganian, Jane A., Forbes, G. B., and Case, Dorothy M., Salicylate intoxication in infant and young child, J. Pediat. **30**:129, 1947.
6. Wegria, R., and Smull, K., Salicylate therapy in acute rheumatic fever, J.A.M.A. **129**:485, 1945.
7. Jager, B. V., and Alway, R., Treatment of acute rheumatic fever with large doses of sodium salicylate, Am. J. Med. Sci. **211**:273, 1946.
8. Quincke, H., Zur Kenntnis der Salicylsaurewirkung, Berl. Klin. Wchnschr. **19**:709, 1882.
9. Smull, K., Wegria, R., and Leland, J., Effect of sodium bicarbonate on serum salicylate level, J.A.M.A. **125**:1173, 1944.
10. Hanzlik, P. J., Actions and Uses of Salicylates and Cinchophen in Medicine, The Williams & Wilkens Co., Baltimore, 1927.
11. Guest, G. M., Rapoport, S., and Roscoe, C., Effect of salicylates on electrolyte structure of blood plasma; action of therapeutic doses of sodium salicylate and of acetylsalicylic acid in man, J. Clin. Investigation **24**:770, 1945.
12. Boyle, M. N., Smull, K., and Wegria, R., Effect of sodium salicylate on acid-base balance of blood, Am. J. M. Sc., **3**:31, 1947.
13. Rapoport, S., and Guest, G. M., Effect of salicylates on electrolyte structure of blood plasma; respiratory alkalosis in monkeys and dogs after sodium and methyl salicylate; influence of hypnotic drugs and of sodium bicarbonate on salicylate poisoning, J. Clin. Investigation **24**:759, 1945.
14. Dodd, K., Minot, A. S., and Arena, J. M., Salicylate poisoning; explanation of more serious manifestations, Am. J. Dis. Child. **53**:1435, 1937.
15. Link, K. P., Oberman, R. S., Sullivan, W. R., Huebner, C. F., and Scheel, L.D., Studies on hemorrhagic sweet clover disease; hypoprothrombinemia in rat induced by salicylic acid, J. Biol. Chem. **147**:463, 1943.
16. Shapiro, S., Redish, M. H., and Campbell, H. A., Prothrombin studies; effect of vitamin K upon hypoprothrombinemia induced by dicoumarol in man, Proc. Soc. Exper. Biol. & Med. **52**:12, 1943.
17. Rapoport, S., Wing, M., and Guest, G. M., Hypoprothrombinemia after salicylate administration in man and rabbits, Proc. Soc. Exper. Biol. & Med. **53**:40, 1943.
18. Brodie, B. B., Udenfriend, S., and Coburn, A. F., Determination of salicylic acid in plasma, J. Pharmacol. & Exper. Therap. **80**:114, 1944.
19. Peters, J. P., and Van Slyke, D. D., Quantitative Clinical Chemistry, Vol. II, Methods, The Williams & Wilkins Co., Baltimore, 1932. p. 283.
20. Krasnoff, S. O., and Bernstein, M., Acetylsalicylic acid poisoning, J.A.M.A. **135**:712, 1947.

Spanish Abstract

Tolerancia Y Toxicidad Del Salicilato en Los Niños

Las dosis masivas de salicilato en el tratamiento de la fiebre reumatica ha venido usandose comunmente en los ultimos años, pero ha habido algunas diferencias en recientes reportes en cuanto a la tolerancia de la droga por los niños.

En este estudio se agrupan 19 niños desde ocho meses a 11 y medio años a los cuales se les ha administrado salicilato de sodio y acido acetil-salicilico en dosis de 0.150, 0.125, 0.10 gm. por kilo de peso. Concentracion del salicilato en el suero sanguineo, contenido de carbonico y determinacion del pH, fueron realizadas en este grupo de pacientes en los que los signos de toxicidad fueron observados muy cuidadosamente. Cinco de los seis casos que recibieron 0.150 gm. por kilo mostraron signos de toxicidad, entre los que se destacaron principalmente, laxitud y anorexia. Los niveles del salicilato en el suero se elevaron por encima de 35 mg. por 100 c.c. de sangre, el pH primero se elevo y despues cayo notablemente y el contenido en carbonico cayo al principio rapidamente y despues continuo bajando mas gradualmente. El acido acetil-salicilico parece ser mas toxico que el salicilato de sodio. Dosis de 0.10 gm. por kilo fueron administradas, pero los niveles de concentracion salicilica obtenidos en la sangre fueron mas bajos que los deseados fluctuando entre 19 a 21 mg. por 100 c.c. de sangre. Cuando las dosis de 0.125 gm. fueron administradas el nivel del salicilato en el suero subio por encima de 35 mg. por 100 c.c. y los valores del pH y del CO_2 permanecieron en sus cifras normales en un largo periodo de tiempo.

El salicilato de sodio en dosis de 0.125 gm. parece ser la droga de eleccion para la terapeutica masiva. Los pacientes deben ser cuidadosamente observados a fin de comprobar lo mas tempranamente posible los signos de toxicidad. Si estos aparecen un cuidadoso estudio de la sangre, particularmente dirigido a conocer el pH deben ser realizados. La medicacion alcalina seria unicamente administrada cuando las valores del pH descienden sin preocuparse del contenido en carbonico. Este ultimo puede ser afectado como simple resultado de la perturbacion mecanica determinada por la disnea.

Los salicilatos son principalmente excretados al traves del riñon razon por la cual pueden determinar efectos toxicos sobre este organo en elevada concentracion, ello hace recomendar el mayor esfuerzo para mantener en sus limites normales la funcion renal cuando estamos en presencia de casos de intoxicacion salicilica.

36 Gramercy Park

THE ABSORPTION OF VITAMIN A IN PREMATURELY BORN INFANTS

With Experience in the Use of Absorbable Vitamin A in the Prophylaxis of Retrolental Fibroplasia

By STEWART H. CLIFFORD, M.D., AND KATHLEEN FAHEY WELLER, A.B.
Brookline, Mass.

THE advisability of supplementing the prematurely born infant's diet with vitamin A has been stressed by various authors. Henley, Dann and Golden[1] advise vitamin A supplement because (1) the premature infant has a relatively low reserve of vitamin A in the liver; (2) the premature infant absorbs both dietary fat and vitamin A less efficiently than does the full term infant; and (3) many premature infants on a low vitamin A intake have a low blood plasma level of vitamin A. Lewis, Bodansky and Haig[2] have stated that "low levels of vitamin A in the blood indicates the presence of vitamin A deficiency." Lund and Kimble[3] conclude that vitamin A is either not transmitted or is poorly transmitted from the mother to the fetus and advise that the newborn infant be assured of an adequate supply of vitamin A in early life. Warkany's studies[4] on the effects of maternal vitamin A deficiency in the rat, have suggested the possible role of vitamin A deficiency in the production of the retrolental fibroplasia[5] that occurs in the eyes of some prematurely born babies.

The present study was undertaken to discover the most effective means of administering vitamin A to premature infants. Eighty-six vitamin A absorption tests have been performed on 72 premature infants weighing less than 2500 gm. at birth and averaging 2000 gm. at the time of testing. Forty-two infants received a test dose of vitamin A in oil by mouth.* Forty-one were tested following the ingestion of vitamin A in a vehicle of either alcohol or propylene glycol.† Two infants were tested after intramuscular injections of vitamin A in oils,‡ while one was tested after receiving vitamin A by inunction.

The single measurement method of determining vitamin A absorption described by Pratt and Fahey[6] was used throughout this study. The technic employed for the measurement of carotenoids and vitamin A in the blood plasma and the system of units used to express these values was that described by May, Blackfan, McCreary and Allen.[7]

The original technic for the vitamin A absorption called for the oral administration of 0.22 cc./kg. body weight of percomorph liver oil. We found it difficult to deliver accurately the small volume of oil required when dealing with two and three pound infants. We, therefore, decided to give all premature infants to be tested a standard ingestion of 0.5 cc. percomorph liver oil.

From the Boston Lying-in Hospital, the Infants' and Children's Hospitals, and the Department of Pediatrics, Harvard Medical School.

This paper was accepted by the Society for Pediatric Research for its program at Skytop, Pa., May 1946, but was not read due to lack of time. The content of this paper was discussed and made available to several workers in the field at that time. Subsequently, Lewis, Bodansky, Birmingham and Cohlan (J. Pediat. 31:496, 1947) have referred to this work and confirmed its findings.

(Received for publication January 20, 1948.)

* Percomorph liver oil (Mead Johnson Co.).

† Vipenta (Hoffman-LaRoche Co.); ViSyneral (U.S. Vitamin Corp.).

‡ Vitamin A in Oil (Squibb Co.).

To make sure the premature infant received the desired test dose a syringe and attached gavage tube were filled with the vitamin A preparation and the tube pinched or clamped off. The tube was passed into the infant's stomach and then the desired amount of liquid was displaced accurately from the syringe. From three to five hours later 4 cc. of blood was withdrawn from the infant's antecubital vein for testing.

TABLE I

VITAMIN A ABSORPTION FOLLOWING A TEST DOSE OF 0.5 CC. PERCOMORPH LIVER OIL (35,000 U.S.P. Units)

Case	Weight (gm.)	Age (days)	Time from Test Dose to Testing hrs.—min.	Carotenoids units	Vitamin A "620" units
1	1400	14	3—50	4.5	12.6
2	1400	23	2—45	10.1	15.1
3	1400	28	3—45	6.3	5.2
4	1400	14	4—10	9.6	6.2
5	1430	37	5—30	6.3	2.7
6	1445	16	4	9.4	7.9
7	1460	3	4	10.6	14
8	1460	16	5	7	15.7
7	1490	12	3—15	12.3	25.9
9	1625	7	3—15	7	35.3
10	1700	19	3—40	10.1	10
11	1820	16	5—	8.2	8.3
12	1820	13	4—15	8	10.5
13	1880	77	4—30	5.1	6.2
14	1880	12	4—20	6.3	10.4
15	1880	57	4—30	12.6	9.5
16	1970	5	4	9.9	9
17	2000	16	2—45	3.5	5.9
18	2000	5	4—25	8	7.3
19	2030	35	5	9.4	50.9
20	2030	16	3	8.2	9
21	2060	11	3—45	13.1	11.9
22	2060	13	5	6.3	12.4
10	2090	56	3—32	6.3	6.8
23	2120	3	4	4.7	24.8
24	2120	7	4—10	6.5	8.4
25	2120	?	4—10	3.5	6.9
26	2180	23	4—25	6.3	7.8
27	2180	19	4—20	9.9	18.3
28	2180	9	4	4.5	6.5
29	2180	43	4—32	6.1	7.5
30	2270	11	3—45	5.6	9.7
31	2275	58	4—10	10.1	22.3
32	2290	12	3—15	2.6	15.1
7	2290	50	3—45	7.2	56.4
33	2290	8	4—30	9.4	14.6
34	2320	7	4	6.5	8.4
35	2440	11	4—45	6.8	10.6
36	2500	23	3—15	5.4	4.8
37	2560	8	3—30	6.3	11.2
2	2775	72	4—15	9.9	8.1
1	2850	77	3	4.9	7.7

The vitamin A content of the various commercial preparations used in the tests was determined with the following results:

Name of Product	*U.S.P. Units per CC. Claimed on label.*	*U.S.P. Units per C.C. Actual*
Percomorph Liver Oil	54,780	71,500
Vipenta	8,330	7,900
ViSyneral	6,680	5,780

Vitamin A Absorption Following a Test Dose of 0.5 cc. Percomorph Liver Oil (35,000 U.S.P. Units of A in Oil): The inability of the premature infant to absorb vitamin A following a test dose of 0.5 cc. percomorph liver oil is shown in Chart I and Table I.

Henley, Dann and Golden[1] arbitrarily chose a rise of 29 units or more above the fasting level as indicating good absorption of vitamin A. Using this arbitrary standard only 3 of

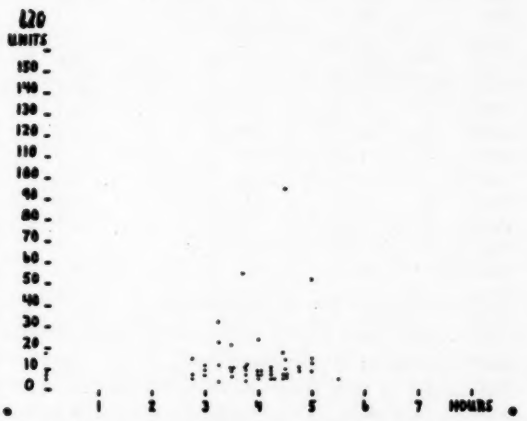


CHART I. Vitamin A. Absorption Following a Test Dose of 0.5 cc. Percomorph Liver Oil (35,000 U.S.P. Units)

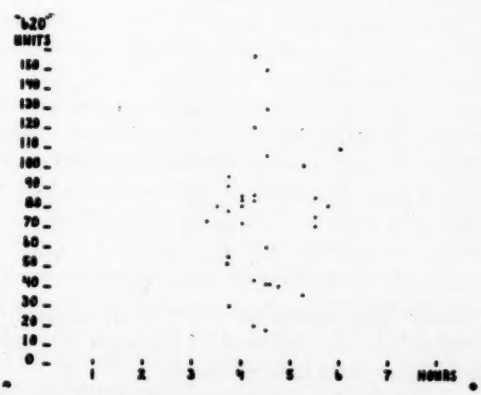


CHART II. Vitamin A Absorption Following a Test Dose of either 2 or 3 cc. Water Soluble Vitamin A (16,000-24,000 U.S.P. Units)

TABLE II

VITAMIN A ABSORPTION FOLLOWING TEST DOSE OF EITHER 2 OR 3 CC. OF WATER SOLUBLE VITAMIN A (16,000–24,00 U.S.P. Units)

Case	Weight (gm.)	Age (days)	Time from Test Dose to Testing hrs.—min.	Carotenoids units	Vitamin A "620" units
38	1335	15	3—20	11.1	72.2
39	1380	14	3—50	8.7	96.1
29	1650	21	4—30	9.2	61
40	1695	11	4—20	6.5	37.1
41	1725	4	4—15	10.4	56.9
31	1740	31	4—30	14.6	157.6
4	1800	38	4—20	14.6	157.6
42	1850	10	4	12.6	131.1
43	1850	16	4	5.5	86.3
44	1880	6	6	7.2	110.6
45	1910	9	4—50	8.9	40.5
46	1910	8	4—27	5.6	41.3
47	1940	11	4—30	4.2	23.4
47	1940	18	5—45	4.2	41.8
41	2060	11	5	7.7	33
48	2060	52	4—30	3.5	18
49	2060	12	5—47	10.6	82.2
50	2060	5	4—38	4.9	41
51	2090	41	4—17	5.1	85.8
52	2090	6	5—15	7.2	101.6
53	2090	12	5—40	5.6	85.2
54	2120	11	4—12	11.1	82.8
55	2150	39	4—13	4	121.8
56	2180	12	5—40	7	75.6
57	2180	9	5—15	7	36.3
58	2180	46	4—35	4.5	58.9
40	2180	18	5—40	4.9	55.4
59	2250	4	3—50	7.2	91.0
60	2250	19	5—30	12.1	69.2
61	2240	23	3—25	5.6	81.8
44	2270	21	4	6.3	81.1
62	2300	9	4—10	8.4	19.3
63	2300	10	3—50	4	28.1
64	2330	27	4— 5	3.3	71.0
65	2330	32	4—30	6.3	130.9
66	2390	5	3—55	5.4	53.7
67	2390	7	3—42	5.8	52.5
68	2450	9	4—12	6.1	42.9
69	2465	6	3—45	5.6	77.4
70	2490	39	4—23	7.7	112.2
71	2490	27	4	10.4	84.1

42 infants (7%) showed good absorption following an unusually large test dose of vitamin A in percomorph liver oil. From three to five hours after the test dose the mean absorption level was found to be 16 units of vitamin A.

Vitamin A Absorption Following a Test Dose of Either 2 cc. or 3 cc. Water Soluble

Vitamin A. (16,000-24,000 U.S.P. Units of A in Alcohol or Propylene Glycol): The ability of the premature infant to absorb vitamin A following a test dose in which the vitamin A is provided in a water soluble form is demonstrated in Chart II and Table II.

Using Henley, Dann and Golden's arbitrary standard, 37 of 41 premature infants (90%) showed good absorption following a relatively smaller test dose of vitamin A in a vehicle of alcohol or propylene glycol. From three to five hours after the test dose the mean absorption level was found to be 85 units of vitamin A.

Three premature infants (Table III) were given absorption tests using oil soluble vitamin A at one test and water soluble vitamin A at another. Using percomorph liver oil the plasma vitamin A levels were found to be 7.5; 22.3 and 6.2 units. Using vitamin A in propylene glycol the vitamin A absorption levels were 61; 157.6 and 157.6 respectively.

TABLE III

	35,000 U.S.P. Units Vitamin A in Oil of Percomorph				16,000–24,000 U.S.P. Units of Water Soluble Vitamin A			
Case	Weight (gm.)	Age (days)	Caro-tenoids	Vitamin A	Weight (gm.)	Age	Caro-tenoids	Vitamin A
29	2160	43	6.1	7.5	1550	21	9.2	61.0
31	2300	58	10.1	22.3	1640	31	14.6	157.6
4	1500	14	9.6	6.2	1700	38	14.6	157.6

Vitamin A Absorption Following the Inunction and Intramuscular Injection of Vitamin A in Oil: Two premature infants were given 30,000 and 20,000 U.S.P. units of vitamin A in oil by intramuscular injection. Three hours later one infant showed a vitamin A level of 7.8 units while 24 hours later the other had an A level of 7.6 units.

One premature infant was given 100,000 U.S.P. units of vitamin A by inunction. Five hours later the vitamin A level in the plasma was 9.3 units.

The Relation of Good Vitamin A Absorption and the Development of Retrolental Fibroplasia in Prematurely Born Infants: Nearly ten years ago we changed from giving the premature infants percomorph liver oil to one of the water soluble preparations. This change was made because of the danger that the infant might aspirate the oil and produce a lipoid pneumonia. Starting at the age of one week all premature infants have received 5000 U.S.P. units of water soluble vitamin A daily. In spite of this administration some of our premature infants developed retrolental fibroplasia. The smaller the infant the higher its chances of developing this condition. In our nursery 23% of all infants weighing from two to three pounds at birth later develop retrolental fibroplasia.[8]

In October 1944 we started giving all of our premature infants at both the Boston Lying-in Hospital and at the Children's and Infants' Hospitals 0.2 cc. (20,000 U.S.P. units) of vitamin A in oil daily by intramuscular injection. This was in addition to the 5000 U.S.P. units given by mouth. The intramuscular injection treatment was abandoned when one premature infant, so treated from birth, developed bilateral retrolental fibroplasia. The infants receiving the intramuscular oil developed areas of induration at the injection sites but had no other untoward reactions.

Comment*

The advisability of providing the prematurely born infant with a readily absorbable form of vitamin A can not be questioned even though the reasons for such an administration are largely theoretical. We can point to no clinical evidence of a vitamin A deficiency disease developing in this group.

We can definitely state that the administration of absorbable vitamin A to premature infants does not prevent the later development of retrolenal fibroplasia. It would seem reasonable to suppose that if this disease is the result of a vitamin A deficiency, this deficiency must be operative in the first six weeks following conception. Should this assumption be correct, then the problem's solution must be sought in improving the potential mother's nutritional state prior to conception.

Since we possess no reliable method of measuring vitamin D absorption comparable to the method available for vitamin A, it is interesting to speculate whether the absorption of vitamin D may not parallel that observed for vitamin A. Should this be the case the provision of vitamin D in a readily absorbable form may be of the greatest practical importance to the normal growth and development of the prematurely born infant.

Henley, Dann and Golden found 40% of their ten premature infants poor absorbers of vitamin A in percomorph liver oil. This is in contrast to 90% of our 42 premature infants found to be poor absorbers. This difference is difficult to explain since in both studies essentially the same methods were used. One factor may have been the larger weight of the Henley group at the time of testing. Two of their infants were very large for a premature group weighing 3400 and 4040 gm. at the test date. Another factor may have been the smaller number of infants studied in their series. However, even if we accept Henley's figure, a form of vitamin A that gives only 60% good absorption can not be considered as satisfactory for the treatment of the prematurely born infant.

Conclusions

Forty-two premature infants were tested for vitamin A absorption after the oral ingestion of 0.5 cc. (35,000 U.S.P. units) of percomorph liver oil. Only three (7%) showed

---

* One member of the Editorial Board in reviewing this paper comments:

"The authors should realize that they are dealing with a single point on the curve of absorption. The slower absorption of A from oil may permit storage of A without such a marked rise in the blood stream as when watery solutions are used. This single point determination is treacherous and full comment on the possible pitfalls and inaccuracies should be included in the comments. IT IS ACTUALLY POSSIBLE THAT AS MUCH A IS ABSORBED FROM ONE MATERIAL AS FROM THE OTHER. They haven't shown conclusively that this possibility is lacking, and should be clearcut in the limitations of the method of study."

It was impossible to make determinations of the vitamin A level at multiple points on the curve of absorption as the premature infant does not lend himself to multiple withdrawals of 4 cc. of blood.

Actually the work of Pratt and Fahey[8] indicated that the single measurement method could be expected to give an accurate index of vitamin A absorption.

Lewis, et al, referred to in the footnote above, found the administration of aqueous vitamin A brought not only higher blood levels than did the oily preparation but considerably *less* vitamin A excretion in the stools. "Thirty-eight (38) percent of the vitamin A intake was recovered in the stools when the oily preparation was administered, as compared with an excretion of 7% following the ingestion of the aqueous product." In animal experiments they found the vitamin A storage in the liver was considerably higher when the aqueous preparation was given.

good absorption levels. The mean absorption level found from three to five hours after the test dose was 16 units of vitamin A.

Forty-one were tested for vitamin A absorption after the oral ingestion of either 2 cc. or 3 cc. (16,000-24,000 U.S.P. units) of vitamin A in a vehicle of either alcohol or propylene glycol. Of these 37 (90%) showed good absorption levels. The mean absorption level found from three to five hours after the test dose was 85 units of vitamin A.

Retrolental fibroplasia could not be prevented from developing in a certain number of premature infants' eyes by the daily oral administration of 5000 U.S.P. of vitamin A in an absorbable water soluble form. Even the addition of 20,000 U.S.P. units of vitamin A in oil by intramuscular injection failed to prevent the development of bilateral retrolental fibroplasia in one infant.

If vitamin D follows the same laws of absorption as does vitamin A, the provision of both A and D in a readily absorbable form should be of great practical advantage to the prematurely born infant.

References

1. Henley, T. H., Dann, Margaret, and Golden, W. R. C., Reserves, absorption and plasma levels of vitamin A in premature infants, Am. J. Dis. Child. **68**:257, 1944.
2. Lewis, J. M., Bodansky, O., and Haig, C., Level of vitamin A in blood as index of vitamin A deficiency in infants and children, Am. J. Dis. Child. **62**:1129, 1941.
3. Lund, C. J., and Kimble, M. S., Plasma vitamin A and carotene of newborn infant, Am. J. Obst. & Gynec. **46**:207, 1943.
4. Warkany, J., Congenital malformations induced by maternal nutritional deficiency, J. Pediat. **25**:476, 1944.
5. Terry, T. L., Retrolental fibroplasia, Am. J. Dis. Child. **68**:75, 1944.
6. Pratt, E. L., and Fahey, K. R., Clinical adequacy of single measurement of vitamin A absorption, Am. J. Dis. Child. **68**:83, 1944.
7. May, C. D., Blackfan, K. D., McCreary, J. F., and Allen, F. H., Jr., Clinical studies of vitamin A in infants and in children, Am. J. Dis. Child. **59**:1167, 1940.
8. Allers, O. E., Personal communication.

Spanish Abstract

La absorcion de vitamina A en los prematuros

Administrando a los prematuros una preparacion oleosa de vitamina A, el 93% muestran una pobre absorcion con limites bajos en la sangre dentro de las 3 a 5 horas de administrales la dosis-prueba.

Administrando a los prematuros preparaciones acuosas de vitamina A, el 90% mostraron una buena absorcion con buenos niveles de concentracion.

Lesiones de fibroplasia no podrian ser prevenidas en el desarrollo de cierto numero de prematuros por la administracion oral diaria de 5000 U.S.P. unidades de una solucion acuosa de vitamina A.

1101 Beacon St.

Pediatrics

VOLUME 1 APRIL 1948 NUMBER 4

AMERICAN ACADEMY OF PEDIATRICS, INC. PROCEEDINGS AND REPORTS

IMPRESSIONS ON PEDIATRIC EDUCATION

By JOHN MCK. MITCHELL, M.D., KATHERINE BAIN, M.D., JOHN P. HUBBARD, M.D.
Washington, D.C.

INTRODUCTION

Quality is one of the most important components of services rendered for child health. While innate ability and on-the-job learning may result in the production of outstanding achievement on the part of an individual or organization, by and large the quality of a given service may be measured satisfactorily by the fundamental training of those who conduct it.

The conduct of child health services comes far from resting solely in the hands of the physician, still further from those of the pediatrician alone. Nevertheless the physician forms, if not the heart, at least an aorta, through which must flow, if but for an instant, the whole volume of child care. Hence the size and strength of the group which constitute such a vessel become a matter of primary concern in a study having to do with the health of children. With this concept in mind, a Study of Pediatric Education became an integral part of the Study of Child Health Services organized by the American Academy of Pediatrics. In undertaking such a study, there was full realization of the importance of other groups as well as of the inseparable interrelation between medical training as a whole and that for pediatrics. Since it was not possible to cover the entire field, the Study confined itself to a survey of the most important segment; namely, the pediatric training of undergraduate medical students and the graduate training of physicians planning to devote their lives to the care and treatment of children.

The field work is complete. It consisted of visits to and surveys of the pediatric departments of 70 medical schools in the United States and of 9 in Canada, the latter carried out by the Canadian Society for the Study of Diseases of Children. Analysis of the material has just started.

STUDENT ENROLLMENT

The problems of student enrollment are not primarily the concern of those engaged in the teaching of pediatrics nor of an organized group of pediatricians, but they are shared equally with other departments and other medical organizations. The quality and quantity of those men who will become engaged in child care either as general practitioners, pediatricians or other specialists are largely predetermined by the processing of applicants to medical schools and by the number admitted.

The present bull market in education has brought to the desks of medical school registrars a number of applications unprecedented in all medical history. Obviously a single individual may

From the American Academy of Pediatrics, Study of Child Health Services, John P. Hubbard, M.D., Director, 2346 Massachusetts Avenue, N.W., Washington 8, D.C.

submit applications to a number of schools and likewise many applicants are scholastically ineligible. On the other hand many schools with geographic limitations on their student body make no record of out-of-area applications. Even after a processing which limits the group to those geographically and scholastically eligible, the ratio of applicants to the number admitted runs as high as 10 to 1 in some schools. This great wave of would-be medical students presages fine things for the caliber of physicians to be graduated within the next few years. Paradoxically it has not always resulted in improvement of those selected. A number of state schools which previously admitted a small proportion of students from other states now accept only those from within their own borders. Those formerly accepted from elsewhere were carefully winnowed and apt to be accepted only if they possessed outstanding qualifications. Under the present system they are lost, to be replaced by those of lower standard from the home state. Further, the mere weight of numbers has at times resulted in a less careful review of the individual applicant. Schools have not all met this crucial and difficult problem with a well-functioning plan.

Much has been said and written in recent months about the need for more physicians. Charges have even been made that the medical profession was purposely restricting the number of graduates. Those who have made such charges are unfamiliar both with the methods and requirements of medical education, and with the fact that present facilities are being stretched to the limit. They fail to understand the inability of the medical school to increase its enrollment in the same ratio as academic departments. The limitations of space, equipment, material and instructors hold the number of students in such courses as anatomy, physiology and pathology to an unexpandable maximum. In the clinical years it is absolutely essential that instruction be carried out in small groups with close supervision and that students have personal contact with patients. This means that there must be an adequate number of beds and patients available per student in the hospital as well as a sufficient number of admissions to the out-patient department. This ratio is already too low in certain schools. Some medical educators believe that the optimal clinical class is 50 students, and that anything above 75 students definitely reduces efficiency. Whether or not this thesis is accepted, certainly too many students cannot be handled properly on the wards where, in addition to the above mentioned features, they interfere with nursing care, or in the out-patient department where adequate space is especially apt to be lacking.

That the 70 medical schools in the United States are doing their utmost to meet the need for physicians while they maintain all-important quality is evidenced by an increase of 17% in the number of graduates in 1947 as compared with the pre-war year 1940. (Based on 54 schools.)

A further increase in graduates results from four new schools recognized during the intervening years. Bowman-Gray School of Medicine at Winston-Salem graduated its first class in 1943; Southwestern Medical School at Dallas and the University of Utah graduated their first classes in 1944; and the University of Alabama at Birmingham in 1946. In addition another school, the University of Washington at Seattle, is expected to graduate its first class in 1950. Two other schools are in the planning stage, the University of California at Los Angeles and the University of North Carolina. An eighth school, the Chicago Medical School, has applied for recognition of its clinical years. Thus, more than a 10% increase in the number of schools has taken place in recent years or is projected in the near future.

Budgets

It is probable that few physicians outside of those immediately concerned fully appreciate the precarious financial situation facing many medical schools today. This is a problem of far-reaching import, which will not be pursued further in this preliminary report.

It is doubtful, too, if many outside of those immediately concerned realize how many clinical departments are operated by a volunteer staff which serves entirely without recompense, or with one so small as to represent merely a token. That good teaching can be done under such circumstances is a measure of the loyalty and unselfish devotion of those called upon to perform this feat. But this same group would be the first to say that, were they provided an adequate budget, one that would allow reasonable part-time pay and thus permit them to spend more time on their teaching duties, this one item alone could immeasurably improve the teaching in their departments.

A suitable budget is not prima facie evidence of good teaching, but by and large the two go together. Even though a plentiful supply of good clinical teachers is available and they are willing to make the necessary sacrifice of time and energy, it is not possible to do the best teaching in the

absence of good laboratory services. The bacteriologist, chemist or pathologist is not so apt to be able to support himself on part-time practice as the pure clinician. The location and nature of pediatric services often require that these persons be paid from departmental funds, especially if they are to be available for teaching purposes. Nor can the correlation between research and good clinical teaching be dismissed lightly. Just as good teaching can be carried on in the absence of a suitable budget, so it can be done in the absence of good research; but again the two usually go together. Under modern conditions it has become extremely difficult to do good research without adequate funds. Funds therefore mean not only research but additional staff to perform the research. Thus, not only is the stimulus of the presence of research staff provided to the clinician and student, but the teaching staff is augmented by them.

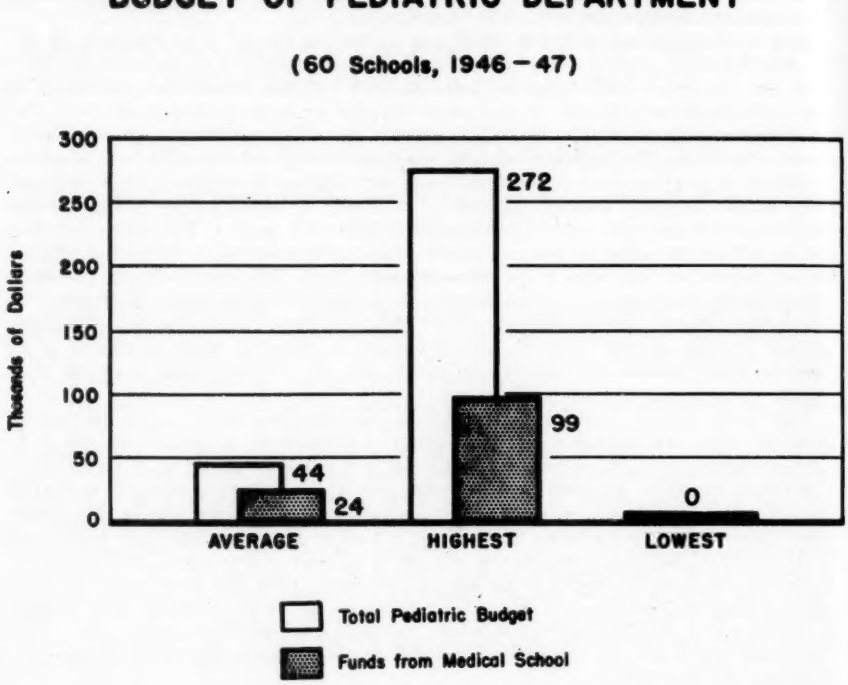


FIG. 1

What constitutes a suitable budget can not be stated in dollars and cents. A large student body necessitates a larger department and a larger budget. The small school located in a metropolitan area, where a considerable number of suitably trained practicing pediatricians are available, can often operate satisfactorily on less budget than a school of similar size located in a small city where few if any pediatricians can be called on for part-time teaching.

There is a wide variation in the budgets of the various pediatric departments (Fig. 1). These run all the way from no budget at all to a top of $272,000, the average being about $44,000. Usually the larger sums will be found to come from grants for research and represent a temporary situation which is not without risk when grants stand in too high a ratio to the amount which can be safely expected from the annual school appropriation. There is not the same divergence when the amount received by the departments directly from the medical school is considered. Here the largest amount so received is $99,000; the average about $24,000.

Since a larger student body requires a larger budget, a comparison of the average pediatric

TABLE I

PEDIATRIC DEPARTMENT BUDGET PER STUDENT IN 55 SCHOOLS

Pediatric Department Budget per Student	Number of Schools
$200 or more	16
100–199	5
50– 99	12
25– 49	8
Under 25	14

departmental budgets in schools of different size is of interest. Table I shows that one quarter of the schools have less than $25 per student in the pediatric budget, while the upper quarter have more than $200 per student.

STAFF

The number and quality of the staff and the amount of time which they give to departmental activities are important items in the success of an undergraduate course in pediatrics.

One-half of the 56 medical schools which have been studied to date have a full-time head of department. (Table II.) In seven instances, heads of departments devote less than one-quarter time to medical school activities.

Twenty-two of the 56 schools have no full-time staff members, and only 19 have as many as five. The average pediatric staff, exclusive of house officers, consists of about seven members giving one-quarter time or more, of whom one-half are on full time.

HOURS IN PEDIATRICS

Many factors must be taken into consideration when any evaluation is made of a pediatric teaching service. As has been indicated, the ability, training, and size of the staff and the aggregate number of hours which they devote to teaching is perhaps the most important single item. But this staff must have under its control a hospital or hospitals which provide a physical plant capable of supplying the necessary beds, accessory services and rooms for student use. These hospitals must be so situated that they can command an ample supply of clinical material for both in-patient and out-patient services. There should be a budget of sufficient amount to insure the stimulus of research activities as well as proper administration of the teaching program. The caliber of the student body, judged on the basis of innate ability and preliminary education as well as on the training which it has received in medicine itself, enters the picture. All of these features may be present in commendable degree, but unless the medical school curriculum assigns a sufficient number of hours to pediatrics, it still will not be possible to give to students the training they need to properly understand the handling of children and the problems of child care. Therefore, the number of hours devoted to pediatrics becomes of paramount importance.

TABLE II

STATUS OF HEADS OF PEDIATRIC DEPARTMENTS IN 56 SCHOOLS

Status	Number
Full-time	30
Part-time:	
$\frac{3}{4}$	3
$\frac{1}{2}$	7
$\frac{1}{4}$	9
Less than $\frac{1}{4}$	7

The number of hours allotted to pediatrics in different schools varies widely, running all the way from 141 to 544 hours. Also, discrepancies have been found between catalogue hours and actual hours. These terms have been coined to allow for the common practice of encouraging or requiring a variable proportion of the in-patient clinical clerk group to be available for evening and weekend admissions. Such hours usually are not shown in catalogues and though they are apt to be less closely supervised than those that are shown, they constitute a valuable adjunct which often represents a considerable addition to total hours. Hence credit has been accorded for time so spent. Students look upon this work as one of the most valuable items of their course, since it permits them intimate contact with immediately ill patients and with the house staff. An oft-repeated student phrase is to the effect that the best teaching not infrequently comes from the man just above you in experience, because he understands what you do and do not know.

TABLE III

HOURS IN PEDIATRICS
IN 59 SCHOOLS

Catalogue Hours in Pediatrics During 4 Years	Number of Schools
400 or more	6
300–399	20
200–299	25
Under 200	8

The variation in the number of catalogue hours in those schools already reviewed is shown in Table III. The average number of hours devoted to pediatrics per school totals 290 catalogue hours and 319 actual hours. Thus, by use of the overtime method just described, an average of 29 hours is gained for each student; and, since a number of schools do not use this system, it is obvious that the average is considerably higher in those schools which do use it.

What constitutes an adequate number of hours for pediatrics will vary with relation to a number of factors, and there is no intention to indicate that it should be identical for all schools. Obviously some departments are better prepared to handle more hours than are others. However, the spread should probably not be as great as four to one where it now stands 544 to 141. When the study of the material is complete, it is hoped that it may be possible to express more definitive ideas on this subject.

A more detailed analysis of hours within the total reveals that there is a wide difference among the various schools with regard to their division by method of teaching. This variation extends to both their absolute and relative number.

In order to better understand the nature of this division and the hours assigned to each category, reference should be made to Figure 2. Here, for purpose of analysis, hours have been separated into two main divisions, the first designated "Didactic" and the second "Clinical Clerkship." Under "Didactic" are grouped lectures, amphitheater clinics, and ward rounds in clinical conferences of every sort. The hours shown under "Clinical Clerkship" represent time spent in working directly with patients, either on the hospital wards or in the out-patient department.

Since the number of hours shown in Figure 2 represents averages only, they give no indication of the many variations found in different schools. Study of the material has not progressed far enough to determine the high and low in each division, but an example will give some idea of the range. The average number of hours spent in purely clinical teaching is 166, among the 58 schools used in the computations for Figure 2. One school has well over 300 such hours. Another school has 28, which means that students will be graduated from this school having received a total of only 28 hours of actual contact with child patients.

It must be clearly understood that the number of hours and the division of time by method of teaching shown in Figure 2 in no way represent optimum or approved figures. For these factual data include schools in which total pediatric hours are obviously insufficient and schools in which work directly with patients is at a minimum.

Those schools in which there exists a broad concept of pediatrics generally provide an adequate number of hours to conduct the course properly. In this concept, pediatrics is that branch of medicine which concerns itself with the entire life of the child from birth to or through puberty. It encompasses every factor which has to do with the emotional and physical growth and development of the child, including environmental, economic and social factors in their relation to disease.

The converse of this attitude is that which looks on pediatrics as having to do with infant feeding, diarrhea, acid-base balance and the exanthems. Naturally there is every gradation between these two extremes, and it is possible for the views of the pediatric staff to be at complete variance with those of that group of the faculty which controls the allotment of teaching hours. Where this situation exists, it is sometimes due to the fact that the pediatric staff is isolated from the rest of the medical school in a physically remote children's hospital.

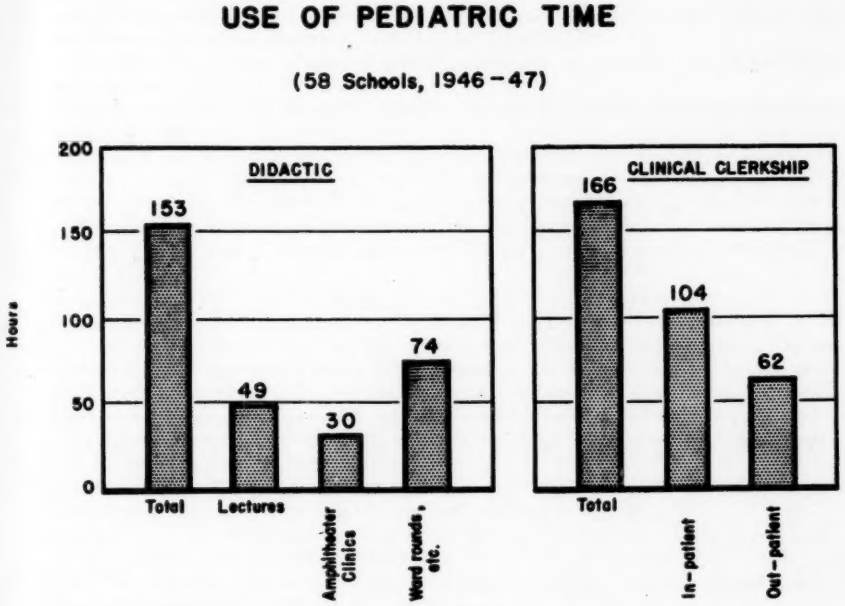


FIG. 2

This thought has been developed on the generalization that, granted a broad concept of pediatric raison d'etre, proper recognition of the specialty would ensue. An old adage which says that all generalizations are false, hence this one is false, holds here; for there exist schools where general and pediatric staff alike possess a broad view of the role of pediatrics but where the hours assigned are inadequate to the needs. Here the lack may be the result of a purely local situation. Occasionally it may be that the pediatric staff is so strongly oriented toward research and house officer training that undergraduate teaching has become of tertiary importance and the necessary pressure to obtain more hours has not been made. More often, however, it is because the pediatric staff is so small that it is already pressed to the limit to cover properly the allotted hours and the budget does not permit the necessary expansion.

Wherever there exists a relative shortage of hours for the proper teaching of pediatrics, the first requisite is that the department itself adopt the broad view of the specialty. Then the department should make a tentative distribution of hours and be prepared to fill them with work which will carry to the student its own reward for time spent. The next step, that of convincing the general faculty of the validity of their position, is often one of great difficulty. Some upper echelon members

of the faculty with a proprietary interest in their own hours, are apt to be resistant to change. In addition, some may have preformed ideas emanating from their own experience which may well have been in a school in which pediatrics has been regarded as of small import.

It should not be our objective to make pediatricians out of students in medical school. It should be our purpose to teach them the norms of emotional and physical growth and development, and the fundamental principles of the diseases of childhood. Then with further study and experience they may engraft on these the ability to evaluate what constitutes a deviation from the ordinary pattern of growth and development of sufficient degree to indicate a pathological change; a knowledge of the procedures which are useful in the prevention of disease; and how to handle children in health and care for them in sickness.

2346 Massachusetts Ave. N.W.

REPORT OF A SPECIAL MEETING OF THE EXECUTIVE BOARD, CHICAGO, FEBRUARY 8, 1948

A special meeting of the Executive Board was held at the Palmer House, Sunday, February 8, 1948, with the President, Dr. John A. Toomey, presiding. There were present Drs. Toomey, Sisson, Stringfield, Beaven, Barba, London, Jr., Munns, McElhenney, Spickard, Hurtado, Grulee, Martmer, Wall, member of the Committee on Legislation—former Chairman of Committee, Wilson, Chairman of the Committee for Improvement of Child Health, Hubbard, Director of the Committee on Study of Child Health Services, Johnston, Chairman of the Committee on Medical Education and Conklin, Chairman of the Committee on Legislation.

A recommendation for Federal support for pediatric education was discussed thoroughly. Changes were made in the original recommendations and the final action of the Executive Board is to be reported to the members of the Academy from the I. C. H. Committee.

The Executive Board voted to give its official endorsement to the First International Poliomyelitis Conference to be held in New York.

A financial report from Dr. Donovan J. McCune, treasurer of the Fifth International Congress of Pediatrics, was read.

It was voted that should a member not pay his dues within the first six months of the Academy fiscal year, that his subscription to PEDIATRICS shall be discontinued until settlement is made.

Dues for Latin-American members were raised from $10.00 to $15.00 a year beginning July 1, 1948.

Dr. Hurtado was authorized to solicit funds from Latin-American branches of United States corporations for the purpose of obtaining money to publish the transactions of the First Pan-American Congress of Pediatrics.

The resignation of Dr. Elmer C. Jackson, Blairstown, N.J., was accepted.

Dr. Martmer discussed at length the matter of the Program for the coming meeting. It was suggested that the Seminars be increased both as to number of seminars and registrants. This was approved heartily. The question of Round Table Discussions was discussed also and in spite of the difficulties involved the present method of conducting them was approved. It was decided to conduct the Presentation of Awards at one session and the Business Meeting at another, the committee reports to be given at the Business Meeting. Dr. Martmer's report was accepted. An evening session for the Latin-American group was approved.

Discussion of School Health Service Bill was then undertaken and the following report from the Committee on Legislation regarding this Bill was presented by Dr. Wall:

Regarding the School Health Services Bills H.R. 1980 and S. 1290, The Committee on Legislation of the Academy met in Dallas in December, 1947, with all members present except Dr. Crawford. The Committee adopted certain principles which it suggested should guide the Academy in endorsing the proposed School Health Services Bill, to wit:

1. That any treatment proposed in any bill should remain within the jurisdiction of private physicians.

2. That appointments to any advisory committees named in legislative bills, as representing organized professional groups, should be from panels of names submitted from such organizations.

3. The Committee felt that the mere publishing of the recommendations of advisory committees annually was not sufficient, but that certain veto powers should be vested in such advisory committees.

4. That expenditures of State or Federal funds for health services should be made to those in economic need.

The School Health Services Bill provides an appropriation of $12,000,000 the first year and $18,000,000 the next year and for such sums afterwards as may be necessary to make health provision for the examination and correction of defects found in school children without such examination.

Regarding H. R. 1980 (Howell Bill) certain safeguards were inserted by its sponsors in keeping with the principles set forth above, some being at the request of the then chairman of the Legislative Committee, and agreed to by the chief sponsor of the Bill, Mr. George J. Hecht. These are:

Page 2, Lines 8-11 reading—Such school health services shall utilize and develop, insofar as feasible, the qualified public health, medical, dental and hospital facilities already established in each community.

Page 2, Lines 17-19 reading—and (especially in rural areas and in areas suffering from severe economic distress) the TREATMENT of such defects and conditions. This phrase in parenthesis was inserted by Mr. Hecht at the request of Dr. Wall, during the early formative stages of the Bill when it was proposed as an amendment of the Social Security Act, Title V which includes this phraseology relating to expenditures from the U. S. Children's Bureau for Maternal and Child Health Services and Services to Crippled Children.

Page 7, Lines 20-23, and (9) provide that the health services described in the State plan shall be available to children without regard to race, color, creed, or nationality, ON A BASIS THAT IS EQUITABLE IN VIEW OF NEED FOR SERVICES. This safeguard as to expenditure of funds to those in need was eliminated by Senator Saltonstall in his Bill (S. 1290), probably at the request of the Children's Bureau through its Chief, Miss Katherine S. Lenroot, who testified as follows at the House hearings:

"Health of School Children, 80th Congress, First Session, hearing on H. R. 1980, page 37—Miss Lenroot, quote: I am very glad that H. R. 1980 does not impose a 'means test' as a condition of making services available within the States. I am concerned, however, that the language of Sec. 6 (a) (9) that the services described in the State plan shall be available on a basis that is equitable in view of need for services might be construed to provide a basis for the several states to differentiate among children on a basis of the economic status of their families. . . . I would suggest that the Committee give special consideration to that phrase."

This testimony was before the House Committee. The Senate has not yet had a hearing.

The implication is justifiable that the elimination of the phrase in question in the Senate Bill, (S. 1290), was accomplished by the Children's Bureau at the behest of Miss Lenroot.

If the Children's Bureau is to administer the funds authorized under the School Health Services bill and the Chief of the Bureau does not read into the text any form of means test, while asking the elimination of phraseology which would provide that the funds be distributed on a basis that is equitable in view of the need for services—which the House Bill (H. R. 1980) indicates is a responsibility of the State administrators, then, in the opinion of the Chairman of the Legislative Committee, Dr. Coursen B. Conklin, and the former Chairman, Joseph S. Wall, the Senate Bill (S. 1290), which will soon reach the stage of hearings, should not be endorsed by the Academy.

In view of the recommendations of the Academy adopted at the Detroit meeting and prior to that at the Cincinnati meeting, the Committee on Legislation feels that the Executive Board might with propriety, acting for the Academy, authorize its representatives, who may be called before the Senate hearing in the very near future, to testify that the Academy would approve the enactment of the School Health Services bill should the following changes in the content of the bill be adopted:

1. That the limited funds proposed should be expended for those in need of treatment services and to those in need who might otherwise be deprived of follow-up services. That the language of the Bill be made more explicit by the reinsertion in the Senate Bill (S. 1290) of the phrase carried in the House bill, (H. R. 1980), Sec. 6 (a) (9), that the services described in the States plan shall be available on a basis that is equitable in view of need for services.

2. That in Section 3 (H. R. 1980), under the term appropriation, page 2, lines 17-18-19 and in S. 1290 in Section 3, lines 19-20, the phrase reading especially in rural areas and in areas suffering from severe economic distress. That is the wording of one of the Wagner-Murray-Dingle Bills.

This change in wording should be insisted upon in the interest of clarity and justice to assure that medical services shall be available on a basis that is equitable in view of need for services.

Provided that the changes suggested above are made in S. 1290, the members of the Committee on Legislation would recommend to the Executive Board that approval be given by the Academy.

* * *

After a great deal of discussion a part of the report from Dr. Harold H. Mitchell, Chairman of the Academy Committee on School Health, was read. (Report follows.) It was decided that this report deserved further consideration and should be submitted to each of the members of the Executive Board for their action. (Since the meeting, the Executive Board has approved this report.)

At the request of Dr. George M. Wheatley the President was empowered to appoint a representative from the Academy to act in the preliminary planning of the Child Safety Campaign which the Metropolitan Life Insurance Company is sponsoring. Meeting adjourned.

THE PRESIDENT'S PAGE

March 19, 1948

DEAR DR. TOOMEY:

I am in receipt of your form letter to all members of the Academy dated March 2, 1948 with the appended report of the American Academy of Pediatrics' "Committee for the Improvement of Child Health."* I note with despair that this report was approved by the Academy's Executive Board, Chicago, February 8, 1948.

I cannot tell you how stunned and staggered I was as I read this vicious document which has received official approval by our Executive Board. I could not believe my eyes. Now that I have recovered from the initial shock somewhat, I wish to inform you of my complete, total, uncompromising disgust with this stupid and visionary report, and the clear implication that control of Academy affairs and of the pediatric survey have fallen into the hands of persons committed to the collectivist social philosophy.

No one is more desirous of the "good life" than I am. No one is more anxious than I for every child in America to have the best of pediatric care and guidance, and an ample share of all the other attributes of a full and abundant life. But only an impractical dreamer could write a report such as this or believe for one instant that adoption of any part of its recommendations could lead to anything but compulsion, coercion, bureaucracy, stateism, and despotism. The report clearly, baldly, and unequivocally cleaves to the communist social philosophy. I don't!

Therefore, please be advised that through my own personal sense of responsibility to the young men and women who choose medicine as a profession, to our honored profession itself, to the American children under my care now and in the future, to the concept of the dignity and worth of the individual, to my conviction that mankind can attain its future high destiny and maintain progress in that direction only through personal liberty under law, I am compelled to proffer my resignation from the American Academy of Pediatrics to become effective immediately, when and if this disastrous report or any part thereof is adopted by the Academy.

Sincerely,

(signed) WM. C. BLACK, M.D.†

---

* Further information from the Committee follows this letter.

† See "The Pediatrician and the Public," page 560, for further comment from Dr. Black.

A FURTHER STATEMENT ON FEDERAL AID FOR PEDIATRIC EDUCATION

SUBMITTED BY THE COMMITTEE FOR IMPROVEMENT OF CHILD HEALTH, APRIL 12, 1948

About a year ago, the presidents of 19 of the country's foremost universities issued a statement on medical education which described in unmistakable terms the gravity of the financial situation now confronting all medical schools. They stated:

"We feel it our duty, as presidents of universities with medical schools, to inform our fellow citizens of the uncertain future of medical education . . .

"Recent years have brought certain notable advances in medical knowledge and care, including penicillin, sulpha drugs and blood substitutes. Those advances may have given the public the impression that future progress in medical care, and the maintenance of high qualitative standards in medical education, are assured.

"Such is not the case. New hospitals and clinics, new drugs, medical insurance plans and state subsidies to medicine do not themselves assure proper medical care. They must be wisely used by an adequate number of skilled physicians. It is only through the hands and minds of men and women trained by our medical schools that society can be given sound medical care and new developments utilized. *The future of medical care and public health depends upon medical education.*

"The present provisions for ensuring a continuing supply of well-trained physicians are inadequate. They are inadequate because the medical schools which provide that supply are inadequately supported in terms of future needs. Few if any of the seventy recognized medical schools in the United States can be confident, with present resources, of maintaining in the future their programs at the essential high level. . . .

"Unless existing conditions are quickly changed, medical education will decline in quality, and medical research will falter."

Those who attended the recent Congress on Medical Education and Licensure in Chicago (February 8-10, 1948) heard ample testimony on the crisis in medical education and how it might be met. Dr. Alan Valentine, President of Rochester University, said in effect:

"Financially, the situation of our medical schools is desperate. It is no longer a question of finding funds to *expand* medical schools, but simply to maintain them as going concerns. . . .

"There is serious talk of Government subsidies to help medical education. I believe such subsidies are inevitable; for even if medical education is wholly successful in securing needed support from private sources, it cannot be successful in time to save our medical schools. Government support has great potential dangers. But the present issue is not whether to accept Government aid, but to work out terms by which it can be provided without permanent ill effects. It behooves us to work quickly and affirmatively to formulate those terms."

To such authoritative statements may be added some of the findings of the Academy's Study of Child Health Services and Pediatric Education, preliminary reports of which were given at the annual meeting in Dallas, December 1947. (See March number of PEDIATRICS.)

The inadequacy of teaching budgets is especially evident in pediatric departments. The total funds available to pediatric departments from all sources are less than $10,000 annually in 21 of the 70 schools. Nine of these have less than $5,000; three have virtually no funds.

Hospitals also are facing increasing deficits and less able than in former years to pay adequate salaries to interns or residents. Meanwhile, specialty boards have demanded longer and longer periods of hospital training. During the past few years, the G. I. Bill of Rights has greatly ameliorated the inequities of this situation and has allowed recent graduates to prolong their hospital training. But now both the number of these individuals who are being subsidized by the Government and the revenue which they bring to medical schools and hospitals are decreasing daily. What will happen when this present source of Government subsidy is withdrawn?

Dr. John McK. Mitchell has collaborated in this report. He is a person especially well qualified to judge this subject on the background of 20 years in the practice of pediatrics and two years spent in personal visits to all medical schools while conducting the Academy's Study of Pediatric Education.

General practitioners are responsible for most of the medical care and health supervision of the nation's children, but relatively few have had special training in this service which constitutes about a third of their day's work. Lectures, clinics, and seminars have all been made available to keep the practicing physicians abreast of the advances in medicine. For the practitioner in areas distant from medical centers these methods have two faults: they can but rarely take the form of bedside teaching and they require that the physician absent himself from his practice. The latter is difficult for any busy doctor and especially so in areas where physicians are few and far between.

In metropolitan and adjacent counties there are four physicians to every 1,000 children, while in rural and semi-rural counties there are less than two physicians for the same number of children. Three quarters of all pediatricians practice in cities of 50,000 or more persons. Other medical services are distributed in like proportion.

Efforts to solve these problems are being made in many places. The 27 schools supported in part by state or municipal governments have received marked increases in budgets in some instances. There are 43 schools, however, which are entirely dependent upon endowment, private gifts and tuition fees.

Of the total budget for medical schools, tuition fees provide less than 28%. The mounting costs cannot be met by placing a greater burden on students. Tuition fees are already as high as most students can pay. Income from endowment seems likely to remain low and there seems little hope that private philanthropies can be counted on to meet the needs of medical schools.

Foundations are supporting several projects under which residents rotate from medical centers through hospitals in small communities. The total number involved however is small.

Five states offer scholarships to students who will agree to practice for definite periods in areas of need within the state. Again the efforts are laudatory but scattered and restricted.

Nowhere is there an overall, nation-wide plan aimed at meeting these crucial problems. It seems inevitable that the Federal Government alone is in a position to finance and administer a program of the scope required.

Review of Recommendations

In the light of such considerations a three-fold plan was evolved to meet a three-fold problem: (1) to strengthen undergraduate pediatric education, (2) to aid graduates and postgraduates who wish added training in medical care and health supervision of children, and (3) to aid in the more even distribution of physicians well trained in the care of children. After detailed consideration of pediatric department budgets and hospital residencies a total Federal appropriation of $5,000,000 a year was recommended.

Section I—Support of Pediatric Education: It was proposed that $2,500,000 be allocated to medical schools for basic budgetary needs of the pediatric department. This would provide $20,000 for each department, the balance to be distributed on the basis of the size of the student body and special needs. It would furnish unrestricted funds needed so sorely to provide salaries for teaching staff. Consider for a moment what this would mean to the 21 schools whose total budgets average $5,140, and to the 10 schools above these whose budgets average $13,924. It would be particularly valuable in increasing the number of part-time teachers and providing due recompense for their essential services.

Grants would be made only upon request from the school; no school need accept this money if it does not feel the need or wish to do so.

Section II—Grants to Hospitals for Pediatric Fellowships: It was proposed that $1,500,000 be allocated to hospitals for the purposes of establishing pediatric fellowships. This in a sense extends the G. I. Bill of Rights in point of time but restricts it to the field of pediatrics.

No hospital is required to establish such fellowships. No physician need accept a fellowship if he does not wish to do so.

An important feature of this section provides for periods of rotation from medical centers to affiliated hospitals in outlying communities. Such rotation might average three or four months. It is believed that this plan offers great and mutual advantages to the resident and to the smaller hospital.

At the resident or assistant resident level of training the house officer is especially proficient in the application of modern methods of diagnosis and therapy to acutely ill patients. On the other hand his experience has been limited in the interplay of social, economic and environmental factors

in their relation to disease. He must still gain skill in the handling of anxious relatives and in the planning of convalescence. In spite of these drawbacks he can be a valuable teacher and is widely used for undergraduate and intern teaching within the limits of his experience.

The weaknesses of the resident are the strong points of the veteran practitioner, whether country or city disciplined. The strong points of the resident are the weaknesses of the practitioner removed from direct contact with medical centers. If the two can be brought together in a favorable environment, great benefit should accrue to both. The rotation service offers such an opportunity.

Section III—Pediatric Fellowships for Graduates Committed to Practice in Areas of Need: It was proposed that $1,000,000 be allocated to states in order that they may establish hospital fellowships in pediatrics, acceptance of which commits the recipient to return to the state to carry on private practice in designated areas of need.

Through this provision, physicians training for general practice as well as pediatrics may be given experience in the care of children before undertaking practice in areas of physician shortage. It is hoped by this means to partially fill the gap until more general measures produce the trained men who will eventually distribute themselves throughout the country.

Acceptance of these fellowships is by free choice of the physician who wishes to participate. Careful thought was given to the question as to whether the physician should be required to pay back the amount of his fellowship in cash, or whether his obligation would be met in terms of service. It was provisionally agreed that this was a matter which should be determined by the appropriate state authority in the light of the experience of those five states which already have such a plan in operation.

Section IV—A Council on Pediatric Education: It was proposed that a Council on Pediatric Education be created consisting entirely of physicians and representing both the Academy and the pediatric departments of medical schools. The function of this Council would be to control the allocation of grants and to assure that Government funds should not bring with them dictation over the policies or practices of the recipient institutions. No grants would be made except with the approval of the Council.

Any expenditure of Federal funds must necessarily be administered by a Federal agency. Much discussion revolved about this question and many persons were consulted. It was finally agreed that neither the U. S. Children's Bureau nor the U. S. Public Health Service should be named as the administrative agency, but that the matter should be determined by the Federal Security Administrator whose agency includes both the U. S. Children's Bureau and the U. S. Public Health Service.

Summary of Response

It should be noted that before action was requested of the Executive Board, consultations were held with heads of pediatric departments, deans of medical schools, the Secretary and General Manager of the American Medical Association, members of the A. M. A. Council on Medical Education and Hospitals and the President and Executive Council of the Association of American Medical Colleges.

Immediately following the meeting of the Executive Board on February 8, 1948, and in accordance with the wishes of the Board, a copy of the recommendation as approved, was distributed by the Committee for the Improvement of Child Health as follows: to the office of the Secretary for distribution to Academy membership; to State Chairmen (U. S. only); to all heads of pediatric departments of medical schools; to chiefs of pediatric services of all hospitals approved for pediatric residencies; and to others especially concerned.

As of present date, 25 or half of the State Chairmen, have replied to the office of the ICH Committee. Of this number, 21 approve the recommendation; two disapprove pending modification; two, co-chairmen of one state, are vigorously opposed. A number of these State Chairmen replied only after conferring with a number of members in their state.

Replies have been received from approximately half of the chiefs of pediatric departments of medical schools throughout the country. All, from whom word has been received, are wholeheartedly in favor of the recommendation with the exception of one who raises certain questions in relation to the administration of the program in the medical school.

Replies have been received from approximately 30 chiefs of pediatric services in hospitals approved for pediatric residencies. All but four of the group have voiced their strong approval of the recommendation.

From the deans of medical schools, a very heartening degree of support has been received.

The Executive Committee of the Pediatric Section of the A. M. A. has given its unanimous approval. Under date of March 16, 1948, a letter was received from Dr. Oscar Reiss, Chairman of the Section on Pediatrics of the A. M. A., from which the following is quoted: "I have received replies from the other members of the Executive Committee of the Section and we all heartily endorse the plan, so that you may take this as the official action of the Pediatric Section of the A. M. A. If I can be of further service to you in furthering the cause, do not hesitate to call on me."

Specific Criticisms

From some of those referred to above, and from other individuals, specific criticisms have been received. They have been summarized below together with comments which appear pertinent.

(1) "The ICH Committee jumped the gun in bringing out recommendations for action before the report came out." The ICH Committee was appointed nearly two years ago and charged with the responsibility of making recommendations for action based upon the Academy study. Preliminary reports of the study were given at the annual meeting at Dallas December, 1947. By that time all of the 70 medical schools had been visited. Reliable, although incomplete results reviewed at that meeting, indicated that first attention should be given to the gross inadequacy of financial support for pediatric education. Without increased provision for the training of undergraduates and post-graduates, pediatricians, and general practitioners, other approaches toward the improvement of child health appeared blocked.

In so far as preliminary findings were released at Dallas, results of the Academy's study became public property. Government agencies, and a specially formed committee of the American Public Health Association have been as eager as the Academy to use the findings of the study to support their objectives. There has been from the outset some concern that our hard-won results might be used by others prior to formulation of our own recommendations resulting from the study. The ICH Committee with the support of the Executive Board has assumed that their responsibilities to the Academy membership dictated prompt action.

(2) "This recommendation opens the door and lets the Federal Government into the field of medical education." The door is already wide open. Federal grants are now being made directly to medical schools for teaching purposes under provisions of the National Cancer Program, the National Mental Health Program, and the National Tuberculosis Program. These programs have been reviewed in the March issue of PEDIATRICS under the heading of "Trends in Health Legislation and Administration." It is obvious that the recipient medical schools have derived great benefit from these grants, otherwise why would grants to medical schools continue to increase? They are made only upon request from the medical schools and the requests far exceed the available funds.

Certain criticisms have implied that the Academy should oppose *all* Federal support for medical education. To do so would mean withdrawing many millions of dollars without which many important projects and certain departments would have to cease functioning. Obviously an untenable position.

(3) "Federal aid to pediatric education will bring Federal control and interference in the teaching policies in the medical schools." The deans and chiefs of pediatric departments would appear to be the best ones to judge this recognized and admitted hazard. They have already had experience with Federal grants to medical schools. It may be assumed that they would be the first ones to oppose any action which would bring bureaucratic dictation in their departments. As shown above they, as a group, strongly support the recommendations and give evidence of the academic freedom which has been preserved under existing Federal grants.

In the opinion of the Committee, any attempt to control the expenditure of these funds, to have them earmarked for one purpose or another, to have them restricted or refused to any medical school because of any requirement other than those already established for the approval of medical schools should be vigorously opposed by the Academy and would certainly be opposed by universities.

Furthermore, it may be said that there is less danger in action along this line than there is in failure to act. The Federal Security Agency has now under consideration broad legislation to aid medical schools. The best chance of assuring that such legislation will not be contrary to medical school interests is to have it flow along a course outlined by the medical profession itself.

(4) "The men who are responsible for the proposal are largely in the teaching group." Five out

of the nine members of the ICH Committee are in active practice; all of the members of the Executive Board are in active practice.

(5) "The council of nine members proposed in the recommendation makes no provision for members in private practice and would serve as a rubber stamp for the Federal Security Administrator." The council of nine as proposed would include three members nominated by the Academy itself, an additional three members who are heads of pediatric departments of medical schools, and three more members who also would be physicians. All would inevitably be members of the A. M. A. It is inconceivable that such a group would put themselves in a position of being "yes-men" for anybody. Furthermore, it is essential to the recommendation as proposed that this Council on Pediatric Education constitute the keystone of the whole program.

(6) "We cannot at any time sanction the right of the government to dictate to any member of the profession how and where he shall practice pediatrics." This sentence obviously refers to the provision in the proposal under which a graduate from an approved medical school would have the privilege of applying for a fellowship in order that he might acquire the necessary training before returning to practice in an area of need within the state receiving the grant. If such a provision is distasteful to an individual he can leave it alone. This certainly is no infringement on individual rights.

(7) "The ICH Committee took action in the field of interest of the Committee on Legislation and the Committee on Pediatric Education." It is a fact that the Chairmen of these two committees, and also Dr. Wall, former Chairman of the Committee on Legislation of the Academy, attended the meeting of the Executive Board on February 8 and concurred in this action.

(8) A bulletin, published by Mrs. Marjorie Shearon, contains a misquotation in reference to the Academy's recommendation. Mrs. Shearon, in reporting on the testimony given by Dr. Hubbard on the School Health Services Bill before the health sub-committee of the Senate Committee on Labor and Public Welfare (to be published next month in this Journal), includes the following words in bold face type within quotes:—" 'Not all of us share the American Medical Association's philosophy of fear of socialized medicine,' said Dr. Hubbard." No such statement was made as will be evident when the report of the testimony is made public. In a subsequent issue of her bulletin (April 2, 1948) Mrs. Shearon generously admits the mistake and offers her apology to the Academy and to Dr. Hubbard for having published an inaccurate statement.

(9) "What and who is the Association of American Physicians & Surgeons, Inc.?" It is apparent that many have confused this organization with the National Physicians Committee whose efforts have been repeatedly endorsed by the House of Delegates of the American Medical Association, or the Committee of Physicians for the Improvement of Medical Care, Inc., whose communications, although dignified and thoughtful, have many times not agreed with AMA opinion on medical care. The Association of American Physicians and Surgeons is a less well-known group which Dr. Fishbein has described as follows:[1]

"The American Association of Physicians and Surgeons has, according to fairly well substantiated rumor, received $10 from each of 6,000 physicians who have subscribed to its principles. Just what it has accomplished other than to state its objectives and to get them out in the press is not clearly apparent. This group, however, proposes that the physicians of the United States strike against the sick public in case the government of the United States should establish compulsory sickness insurance. Such an action would be contrary to all of the traditions of medical science covering the responsibility of the physician to the sick. No official body of the American Medical Association has ever ventured even the thought that physicians would neglect to administer to the sick as evidence of their opposition to the law of the nation."

Conclusion

The Executive Board and the Committee for the Improvement of Child Health have proposed this plan as a coordinated, nation-wide effort directed at the heart of the problem, the assurance of a steady and nationally distributed supply of qualified physicians, well trained in a field of great need. They have agreed that the Federal government is the only agency which can be expected to finance and administer a program nation-wide in scope. The plan provides adequate safeguards for the maintenance of complete academic freedom by the medical schools. A National Advisory Council

[1] J. A. M. A. 130:512 (Feb. 23), 1946.

of nine physicians would be in a strategic position to oversee the administration of the law. Acceptance of funds by schools, hospitals and individuals would be entirely voluntary.

There are no startling new avenues opened by this program. The Federal Government contributes 80% of the budget of one medical school, makes grants directly to medical schools for teaching purposes under the provisions of successfully operating programs, and contributes to a number of others through grants and fellowships for research. Among these are 13 pediatric departments which receive direct government grants of some sort. In addition, 27 schools are largely tax supported by funds from states and municipalities.

The principle of an individual receiving a specialized education, in return for which he gives certain years of service is as old as the United States Military and Naval Academies. It is in operation in medicine now in five states and through several foundation grants.

There are advantages to starting such a program in one field only. By doing so it becomes possible to study the problem through the actual operation of a plan which is restricted in cost and scope. If it proves unsatisfactory it can be abandoned without too great dislocation. If it is successful, there can be formulated a more comprehensive plan based on experience which has been gained.

Respectfully submitted,

Committee for the Improvement of Child Health

JAMES L. WILSON, M.D., Chairman
JOHN P. HUBBARD, M.D., Director
LEE FORREST HILL, M.D.
ROGER L. J. KENNEDY, M.D.
HENRY G. PONCHER, M.D.
GROVER F. POWERS, M.D.
WARREN W. QUILLIAN, M.D.
H. E. THELANDER, M.D.
CLARENCE H. WEBB, M.D.
GEORGE M. WHEATLEY, M.D.
Ex-officio: JOHN A. TOOMEY, M.D.
WARREN R. SISSON, M.D.
CLIFFORD G. GRULEE, M.D.

Special Reports

SPECIAL REPORT FROM THE COMMITTEE ON SCHOOL HEALTH TO THE EXECUTIVE BOARD

Two of the greatest weaknesses of school health programs are involved in serious controversies that have interfered with obtaining federal legislation for meeting needs where state and local funds are inadequate for satisfactory services.

First, there has been a failure in team work between educators and public health personnel, "Doctors are told what they should do by people who do not know what a doctor can do." Medical and nursing services have failed in their educational objectives. Educators and medical personnel have worked independently on the same children as if each child was sharply divided into mind and body. Very little joint planning has been done by the two professions to solve the problems of children and their development. This failure in team work has been the result largely of a continued rivalry over jurisdiction as to who will spend the money, who will have the power, and who will receive the credit. The two great professions of education and medicine have only occasionally, here and there, learned how to use the great resources of the two professions to serve children.

Second there has been the frequent failure to get something done for the children in need of medical service. Often the trouble is merely a failure to use the medical facilities that are available in the community. Not infrequently the trouble has had its origin in inadequate education as to how to use those facilities. But the big controversy has been over the question of whether all medical services will be free to all children regardless of ability to pay, or whether a prepayment plan for medical care will be compulsory or voluntary, and whether the federal government will control the funds and pay the physician or whether each community will work out their own plan for making medical service available to all. These problems, of course, can not be divorced from the aims and efforts of the medical profession to improve the knowledge and skill of the physician and the development of laboratory and special diagnostic facilities so that they may be available as needed. Any progress made in extending medical facilities to care for those who might benefit and in the improvement of the quality can come only through agreement rather than through continuing the controversy.

Your Committee on School Health has indicated one important way that the work of the physician in the schools can contribute to pediatric health supervision and post graduate medical education. The further improvement of the quality of medical service can come only through such comprehensive plans for medical education and post graduate facilities as can be developed by the profession.

In line with the recommendation of the Academy's Committee on School Health that federal legislation might make an important contribution to the health of school children, the School Health Section of the American Public Health Association has drafted a series of principles (See Public Health, Nursing and Medical Social Work Section) which provide a basis for legislation that avoids these two controversies. As these principles appear acceptable to both sides of both controversies, it seems pertinent that the Academy should consider the principles in advance of the drafting of any specific bills to be presented to Congress. If these principles are acceptable to the Academy, then we might well insist that the legislation proposed may conform to these principles.

HAROLD H. MITCHELL, M.D., *Chairman*

SPECIAL REPORT FROM THE COMMITTEE ON RHEUMATIC FEVER

There is such a high level of interest in rheumatic fever in the Academy, as evidenced by the attendance at the Rheumatic Fever Luncheons and at Round Table Discussions on this subject the past three years, that the Committee on Rheumatic Fever believes a special report to Academy members on recent organizational developments in this field would be timely.

MEMBERSHIP IN THE AMERICAN HEART ASSOCIATION

The American Heart Association has completed during National Heart Week a successful drive for funds to support its research and educational program and those of its local affiliates. No doubt some Academy members were involved in their own communities' participation in this nationwide

activity. Since rheumatic fever is a substantial part of all heart disease, pediatricians should take an increasingly active part in efforts to combat the cause of heart disease. Your Committee urges Academy members to join their local heart associations and the American Heart Association. We feel that it is most important for pediatricians—who see this form of heart disease, in its early stage, who also are often the first to recognize congenital heart disease and who understand and practice the principles of preventive medicine—to be in the vanguard of the movement to fight heart disease.

Rheumatic Fever and the School Child

This is the title of a joint statement on rheumatic fever by the Committees on School Health and Rheumatic Fever to guide school authorities in the understanding and management of the disease through the schools. The statement has been approved by the Executive Board and will be sent to all members of the Academy. The Committee on Rheumatic Fever believes that State Chairmen should take responsibility for circulating the report to the proper authorities in their states.

Film on the Diagnosis of Rheumatic Fever

The Mead Johnson Company has offered to produce a motion picture on rheumatic fever, and has invited your Committee to prepare a script. This is being done. At the Dallas meeting, a first draft was reviewed by the Committee. It is hoped to have the picture completed by the next annual meeting of the Academy.

Rheumatic Fever Teaching Centers

Your Committee at a meeting of the Rheumatic Fever Advisory Committee of the U. S. Children's Bureau stated as its opinion that "Rheumatic fever training programs should be set up under departments of pediatrics, with the immediate teaching being done by teachers selected because of their knowledge of rheumatic fever and not necessarily because of their training in pediatrics or cardiology." The Committee recommended communicating with Dr. Martha Eliot because it believed more funds should be allocated to the development of training centers for rheumatic fever. Accordingly, the Chairman expressed this thought in a communication to Dr. Eliot, to which she replied: "I know that Dr. Daily is exploring carefully the questions of training centers for workers in the rheumatic fever programs. We have felt that it was wise to start with one and expand as fast as is possible with the resources at hand. We are glad to have this expression from your Committee."

Study of Rheumatic Fever Programs

The Committee also recommended to the Executive Board that a study be made of private and public rheumatic fever programs and that the Committee on Improvement of Child Health be requested to consider effecting this study.

Future Objectives of the Committee

The future objectives of the Committee, from what has been described of the activities, fall into two categories: (1) Professional education, (2) Appraisal of current programs of service. With respect to the former, our film on the diagnosis of rheumatic fever, together with the statement of Rheumatic Fever and the School Child would be useful contributions. We also feel that the Children's Bureau should be encouraged to support teaching programs wherever possible and we urge all pediatricians interested in the problem of rheumatic fever to participate in their local community rheumatic fever programs, especially supporting local heart groups, and improving the school health program.

American Council on Rheumatic Fever

As you know, the American Council on Rheumatic Fever was formed in 1944 under the egis of the American Heart Association to act as a central clearing house on educational programs for professional and lay groups and to foster research. Dr. Charles A. R. Connor is the Medical Director. His office is located at 1790 Broadway, New York 17, N.Y. The current drive for funds of the American Heart Association promises to bring funds into the Council on Rheumatic Fever so that its program may actually be implemented in a substantial way for the first time. The Academy is represented on the American Council on Rheumatic Fever by Dr. Hugh McCulloch and Dr. Alexander T. Martin, both members of the Committee on Rheumatic Fever. Your Chairman also is a

member of the Council as a representative of the Executive Committee of the Council and is Treasurer of the Council.

Other Interesting Developments

Another development of interest is the Helen Hay Whitney Foundation for Rheumatic Fever Research which was established by the Whitney family in July 1947, with a five million dollar endowment for the purpose of aiding rheumatic fever research. Dr. T. Duckett Jones of the Good Samaritan Hospital in Boston is the Medical Director pro tem. He is an associate fellow of the Academy. The Foundation's address is 525 East 68 Street, New York City.

In 1945, 151 life insurance companies in the United States organized the Life Insurance Medical Research Fund and made available approximately $500,000 a year for research. Cardiovascular disease has been selected as the first area to which funds will be allocated. Since 1945, almost $200,000 has been spent from these funds on rheumatic fever research. Dr. Frances R. Dieuaide, former Professor of Medicine, Harvard Medical School, is the Scientific Director. The fund is located at 2 East 103 Street, New York City.

George M. Wheatley, *Chairman*

SYMPOSIUM ON PUBLIC HEALTH

Public Health and the Pediatrician, Knox E. Miller, M.D., District Director, U. S. Public Health Service, Federal Security Agency, Dallas, Tex.

The era in which we live is one characterized by superlatives. Within less than an average life span have been crowded into human experience more epoch making developments wrought by human instrumentalities than in any dozen life spans in previous history. Though too familiar to you all to require recounting, they may be classified in general as measures and devices for labor saving and mechanical perfection, speedy communication and transportation, life conservation and life destruction. The recent war brought forth unparalleled refinement in methods for destroying human life, while medical science has been equally industrious in devising ways and means for health protection and life saving. The former enterprise we hope to see held in abeyance but the latter can and must continue on in its triumphs over the yet unresolved mysteries and obstacles.

Of all the colossal human achievements within our era there is none so impressive as the downward trend of morbidity and mortality. From a general death rate in the registration area of 17.2 per 1,000 people in 1900 it has sunk to approximately 10 at the present time. Coincident with this there has been an increase in the life span from 49.25 years to about 65. Translated into more familiar terms, these figures mean that, if the death rate of 1900 had prevailed in 1946, in a population of 143,000,000, there would have been 1,029,600 more deaths than actually occurred during the latter year, or an annual saving of more than 1,000,000. Also the lengthened life span means that every group of 100,000 persons can look forward to 1,575,000 more years of life than a similar group in 1900.

Of the many other thought provoking achievements, a few more will be mentioned. Since 1900 tuberculosis has dropped from second to seventh in the causes of death in the United States. As late as 1935 its mortality rate was 55.1 per 100,000 population. In 1945 it was 40.1. Up to 1940 only 10% to 15% of admissions to tuberculosis hospitals were minimal cases. Today, with modern case finding techniques, 65% to 70% of all cases found are minimal. Typhoid fever, diphtheria and smallpox are approaching the vanishing point. But perhaps of more immediate interest to this group is the fact that thirty years ago 100 out of every 1,000 infants died in the first year of life; whereas, in 1945 the number was only 38.3; also the fact that since 1935 the average loss of mothers in childbirth has declined from 5.8 per 1,000 live births to 2.1.

The greatest single factor in reduction of the general death rate and the lengthened life span has been life saving in the years of infancy and early childhood. Since this is the period of life in which members of this audience are primarily concerned, the position occupied by the pediatrician is unique with respect to the objectives of public health. It is, therefore, not surprising that the pediatricians should be the most acutely health conscious of all groups engaged in medical practice. The pediatric survey undertaken by your organization last year is a splendid manifestation of your purpose to ascertain the facilities for meeting the pediatric problems and the degree to which these problems are being met. With such basic information you are in a position to coordinate your forces with those of the public health agencies in an intelligent and effective manner.

Evolution of Public Health: Like the human organism, public health has had its infancy and childhood. It may now be considered to be in the adolescent period. Being a product of medical and allied sciences, it could not at any period of its history rise above the level of such sciences. Its first conception was to prevent contagion by means of isolation and environmental sanitation. The former, while still in use to some extent, represents largely an altar to an unknown god. Sanitation continues to be one of the foundation stones of the public health structure. The child along with other members of the family must have a safe water supply, safe milk and food supply, safe sewage and refuse disposal, freedom from disease bearing flies, mosquitoes, and other insects and vermin, and hygienic lighting, heating and ventilation.

The next potent weapon to appear in the public health arsenal was immunization, of which smallpox vaccination was the first example. The extensions in this field are well known to you all, and of

From the Annual Meeting of the American Academy of Pediatrics, Dallas, Tex., December 8-11, 1947.

course the range is still widening. The more recent trends have been directed against disease entities or disease groups such as venereal diseases, tuberculosis, cancer, mental disorders and behavioristic problems, nutritional disorders, and dental problems. Over all and under all is public health education. A review of the foregoing activities readily reveals the fact that to a large extent they have to do with children, but the mistake of predicating a health service entirely based upon children and mothers should not be made.

The propriety of classifying the foregoing functions as public health duties would raise little question in any locality. They would ordinarily be considered orthodox public health activities. There is a growing conception, however, that these do not constitute all of the public health obligations. It must be admitted that there is a vast reservoir of illness which is undermining the national strength and efficiency, and which goes unattended due to ignorance, neglect, lack of facilities, or inability to purchase private treatment. Undoubtedly the practicing physicians are concerned in a large way with this problem, but should they be expected to carry the whole load of responsibility or should they be assisted by some public agency in meeting the problem?

Your nationwide pediatric survey will reveal to what extent the problem of adequate medical care to children is being met, but since this is one of the major objectives of your survey, it is anticipated that any assistance the public health agencies can render toward this end will be welcomed. The preliminary findings of your survey indicate that in North Carolina the average number of visits per day for the care of children by general practitioners was 25, as compared with 26 for pediatricians. For well children, however, the pediatricians' visits averaged one in three as compared with one in five by the general practitioners. With respect to health supervision of children one to three years of age, seven times as many visits for health supervision of infants and pre-school children take place in the physicians' offices as occur in well child health conferences, and the work of the general practitioner in this connection is four times that of the pediatrician.

Thus, it is evident that the general practitioner, the pediatrician, and the public health worker are all actively engaged in health supervision of children and each group shares in the phenomenal advances that have been made in sickness prevention and mortality reduction. More can, and should, be done. The preliminary findings do not indicate the degree of inadequacy in health promotion and medical care, but it is safe to assume that many children lack these facilities. Public health is ready to join forces with the practicing physicians in extending needed care to all who may be unable to avail themselves of the services of private physicians.

Local Health Organization: The media through which public health principles are applied have evolved along with the program itself. The first continuing State Board of Health was established in Massachusetts in 1878. Primitive local health machinery consisted usually of a physician designated for emergency service in the presence of an epidemic. It was not until 1911 that the first local full time health unit was established, and then only with untrained personnel, since the first school of public health was not established until 1923. The principle of cooperative financing and management of local health service came into being in 1917. Federal participation was irregular and very small up to 1936 when the Federal Security Agency appropriation of eight million dollars was made available for assistance to state and local health services. Since then special appropriations for venereal disease, tuberculosis, cancer control, mental hygiene and industrial hygiene have been enacted, so that the grant-in-aid funds for all purposes including general health but exclusive of aid for hospital construction amounted to $31,924,731 for the fiscal year 1948.

Thus, local health service has progressed to the stage where it occupies a specialized professional status, and employs the services of doctors, nurses, engineers, sanitarians, public health educators, and statisticians. Gone are the days when public health needs can be satisfied by part time physicians called into emergency service to combat epidemics. Public health is now a career service for which the several groups of workers must come equipped with specialized training and experience. The minimum organization through which modern public health can be applied is known as a local health unit. Such a unit must consist of at least a medical officer, one or more nurses, a sanitary engineer or sanitarian, and necessary clerical assistance. From this minimum organization, the composition and size of health units vary within a wide range up to hundreds or even thousands of employees, depending upon the population served, extent of problems, and funds available. There can consequently be no accurate generalization as to what is an average health unit.

In the continental United States there are 3,070 counties. The county is the most convenient

unit of local government upon which to project the needs for health organization. In four instances —Denver, New Orleans, San Francisco, and Philadelphia—the county and city are coincident. In many other localities where there are large cities, separate health jurisdictions are maintained by the city and the county in which it is located. While health service is far below what it should be in most of the large municipal centers, the greater concern is for those areas which have no health service at all. As of June 30, 1942, 1,828 of the counties in the United States were credited with having full time local health service of some description. This represents approximately 60% of the total. The population thus served was approximately 75% of the total. The difficulties involved in extending health service coverage to the remaining 40% of the counties and 25% of the people are out of proportion to those encountered in the coverage already effected. It is like shaking an apple tree. The ripe fruit comes down with comparatively little effort, but the last green apple on the tree requires prodigious effort to bring it down. The problem of achieving complete coverage is being given intensive study and planning. In many instances the difficulty lies in lack of interest. This can be solved by education. In others it is a lack of funds. Here the states can help by a differential subsidy in favor of the poorer communities, but area is a factor about which we can do nothing. Obviously population is a key factor. There are certain population limits below which we cannot go if we expect to maintain effective health service, so that where the population is sparse, it becomes necessary to combine two or more counties in order to include the requisite minimum population. A study made by Emerson and his associates under the auspices of the Commonwealth Fund in 1945 bases its calculations for full coverage of the United States with health service upon a minimum population of 50,000 per unit. It is, however, recognized that there are many single county units operating effectively in much smaller population groups. To obtain a population of 50,000 in sparsely settled areas a combination of as many as five or six counties covering as high as 40,000 square miles may be required. By comparison, the total area of the State of Rhode Island is 1,067 square miles. The enormous areas to be served by large health districts naturally increase the cost of operation tremendously, so that the per capita cost in such instances is much greater than in compact populations.

Programs, Personnel, Laws, and Finances: Complete coverage is a recognized and desirable goal, but that alone is not enough. There are now four States—Maryland, Alabama, South Carolina and New Mexico—plus the District of Columbia, whose entire populations are under the jurisdiction of full time health units, but the extent and character of service performed vary within wide limits. The same is true of health units generally, wherever they may be found. Few, if any, local health organizations, great or small, have a program comprising all of the services which properly belong to public health. In all instances such health programs as are in operation tend to be more or less out of balance. That is, some phases are stressed unduly, while others are understressed, thus violating the principle of relative values.

It is exceedingly rare to find any health program fully manned with competent personnel. In many instances the health unit force is but a skeleton crew. The situation became so acute during the war when large numbers of health workers were drawn into military service that the whole system of local health service would have found it difficult to survive without the aid of medical officers, nurses and engineers recruited by the Public Health Service and loaned to the states for assignment to local health units. It was anticipated that this situation would be relieved at the close of the war when health workers were returned from military service. While it was relieved somewhat, it is far from being corrected, since a large number did not return to their previous jobs. Others more remunerative fields beckoned. Particularly was this true of medical officers, who were attracted by the allurements of lucrative private practice. Also, the salary scales for health workers of all grades differ widely between the states, so that the drift was toward those states offering the greater financial inducements. The natural consequence was that the low salary areas were stripped of their best workers. Adjustments are being made rather generally, but it will be some time before the situation is stabilized.

Whereas public health in its inception was a law enforcing measure, little in the way of police power remains in public health. It functions principally as a community service enterprise. Nevertheless certain phases of public health must have legal sanction, as in the case of sanitary control of milk and food supplies, waste disposal, nuisance abatement, and the regulation of epidemic diseases. Generally speaking, state and local health laws and regulations are antiquated or obsolete

and should be overhauled in accordance with the most advanced public health concepts. In the early stages of local health unit development the health unit itself was illegal, since there was no precedent for it in the existing statutes. They were organized and conducted, therefore, by mutual agreement only. In not a few instances this situation still obtains. In this category, for example, is the great State of Texas, where local authority still resides in part time local health officers. Legally, the local health unit does not exist. In the New England States local health service has encountered many difficulties because the unit of local government is the town or township rather than the county. To a large extent similar difficulties have retarded local health service in the great States of Pennsylvania, Wisconsin, and Minnesota, and Iowa. Illinois was in this same situation up to 1944 when a realistic and modern local health law was adopted. Since that time it is interesting to note that Illinois has made more rapid progress in the extension of local health service than any other state.

It is unfortunate that there is no reliable measuring device for estimating the quality of local health service. Neither the per capita expenditure nor the number of workers employed furnishes the index to the quality or even quantity of their output. The best approach to this is by means of a periodic inventory or survey by a recognized authority who knows something of the accepted standards of performance.

Much has been accomplished toward realization of the goal of health service for all, but much remains to be done. It is notable that the local health unit has been universally recognized as the desired standard. This will ultimately be achieved, but in the meantime we must fill up the gaps in existing health units. Programs must be made more complete and better balanced; the number of skilled workers must be multiplied; more money must be invested; and laws must be adjusted so as to facilitate progress in administrative machinery, disease prevention and health promotion. We have not yet measured up to our responsibilities in these fields of endeavor. Until this is done we should proceed with caution toward participation in new fields.

Since the public health program is aimed either directly or indirectly at the early years of life in such a large measure, it should be of peculiar interest to pediatricians. Through your cooperation significant progress can be made toward improvement of existing health services, and toward extending them to unoccupied territory.

Food and Drug Laws; Interpretation and Enforcement, J. F. Lakey, Director, Bureau of Food and Drugs, Texas State Department of Health, Austin, Tex.:

It is indeed a pleasure and an honor to appear before this group to discuss present day legislation which is designed to prevent adulteration and misbranding of food and drugs, a practice with which organized society has been coping since ancient times.

Time will not permit a review of the history of food and drug legislation; however, I would like to briefly mention some of the earlier attempts made to prevent adulteration. In 1316 the spicers of London began to regulate the quality of their produce. Food control laws were passed in France and Germany in the thirteenth century, and in the fourteenth century we find that artificial coloring of butter was prohibited in Paris.

The development of food and drug industries which distribute their products over the entire nation caused many new and serious problems in the safeguarding of the health and welfare of the people. It was clearly evident that the consumer could not judge the quality or fitness of the food or drugs which he purchased. The Supreme Court of the United States has clearly pointed out that food and drug laws are designed to reach phases of the lives and health of people which, in the circumstances of modern industrialism, are largely beyond self-protection.

The first general bill establishing safeguards in food and drugs was introduced in Congress in 1879. This bill was bitterly opposed by those engaged in domestic trade in food and drugs until the Federal Pure Food and Drug Act was passed in 1906. Naturally, when the bill was introduced in Congress in 1906, opposition continued, but the press and an aroused public were behind the fight for effective legislation. The bill was eventually passed and for the first time in history the consuming public was given protection against the greedy and unscrupulous. It is true that the majority of those engaged in the trade in food and drugs do not need regulation. They observe the spirit as well as the letter of existing food and drugs laws; unfortunately, however, there have been a few who put personal greed above the well being of their customers, and who

do not hesitate to enrich themselves and cheat their neighbors by adulterating or misbranding their merchandise.[1]

No one will question the fact that there were serious limitations and omissions in the Pure Food and Drug Act of 1906. Even at that time, economic and social changes were rapid, and it was soon evident that the type of regulations which met the problems of 1906 could not cope with the problems of the subsequent years. Transportation facilities improved; people began to read newspapers and periodicals more widely, thus becoming better informed; the span of life increased; new drugs and mechanical devices for therapeutic purposes were thrown upon the public; vitamins were discovered. These new developments, together with changes in mode of living, were very definite factors and were instrumental in the passage of the Federal Food, Drug and Cosmetic Act of 1938.

While it is not my purpose to discuss the federal law, I would like to point out some of the provisions of the act which were not included in the Pure Food and Drug Act of 1906. A drug is declared misbranded unless its label contains adequate directions for use or if it is dangerous to health under the conditions of use prescribed in its labeling; more informative labeling; control of cosmetics, mechanical devices offered for curative purposes, and devices and preparations claimed to bring about changes in the structure of the body; inspection provisions were added; and more stringent penalties provided for violations. Perhaps one of the most significant sections of the new federal law deals with sanitary conditions under which foods, drugs or cosmetics are prepared, packed or held. The original federal law did not deal directly with sanitary practices but did declare food to be adulterated if it consists in whole or in part of any filthy, putrid, or decomposed substance. Proof of violation under the old law consisted almost entirely on the results of laboratory analysis of samples of food collected, whereas, under the new law, food is considered to be adulterated "if it has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth or whereby it may have been rendered injurious to health".

Naturally, every reputable manufacture of food and drugs is heartily in sympathy with the intent and purposes of food and drug legislation. They realize that the consuming public is entitled to protection against fraud and deceit, and every intelligent businessman knows that it is to his definite advantage to get rid of unfair competition based on economic cheat and fraud. He also knows that public confidence in the soundness and honesty of his product will increase the volume of his business.

Even though the majority of those engaged in the manufacture of food and drugs are willing and anxious to comply with the requirements of our federal and state laws, certain variations in interpretation by both enforcement agencies and inspectors cause considerable concern to those manufacturers. It certainly leads to confusion to be inspected by local inspectors, and having attempted to comply with local ordinances, be visited by state or federal inspectors and find that the changes had not been in compliance with the requirements of the law. This not only leads to confusion, but results in duplication of work, added expense, and tends to destroy public confidence. That condition is gradually being corrected by having representatives from federal and state agencies work with local inspectors. This cooperation between different enforcement agencies results in coordinated interpretations and decisions.

We who are charged with the responsibility for the enforcement of food and drug laws are continually questioned regarding tolerances which may be allowed. Our state law and the federal law state that a food shall be deemed to be adulterated if it consists in whole or in part of any filthy, putrid or decomposed substance. This provision implies that all food must be entirely free of filthy or decomposed substances, which is almost an impossibility insofar as certain foods are concerned. It is true that many foods are agricultural products grown in open fields and are exposed to many types of contamination—ranging from bacteria to insects, etc. In view of this situation, in making interpretations, it is absolutely necessary for enforcement officials to set up certain tolerances within its own organization. By this method, we are able to draw a line between products which we feel are safe and satisfactory and those which are unsatisfactory for human food. While we are fully aware of the problem facing the industries, yet it is obvious that no written tolerance for filth can be publicly stated. Such a published tolerance would, without a doubt, result in careless sanitary practices and procedures and destroy public confidence. We have

not arrived at a period in our history when organized society will permit legislation allowing certain definite amounts of filth in our food. In detetmining whether or not a food is satisfactory for human consumption, we consider the amount and type of extraneous or foreign substance in the particular sample, the condition of the raw products making up the finished food, the sanitary conditions under which the product was prepared, and finally the method of handling from producer to consumer. This policy of interpretation is, I believe, more or less uniform throughout the United States insofar as enforcement of food and drug laws is concerned.

In order to more clearly point out the need for uniformity in food and drug laws, let us consider the existing situation in the milk industry. Perhaps no more than one-half of the cities grade their market milk supplies, with the grade designations including certified, grade A, grade B, grade C, and grade D, selected, inspected, guaranteed, special and market. Some of these grade designations were repeated for raw milk as well as pasturized. There also exists a wide difference from state to state and city to city as to legal standards for corresponding grades as well as frequency of inspections.[2]

Of course, dairy legislation is designed to protect the health of the consumer and to stabilize the dairy industry. Attempting to attain these objectives, legislation has been passed which leads to confusion and in many cases directly interferes with milk distribution. Laws and regulations adopted by states, counties, and cities prescribe in detail the sanitary conditions under which dairy products shall be produced, processed and distributed. The enforcement of these laws and regulations requires inspection, and control is exercised by granting permits to producers, processors, and distributors to sell their product in a given territory only after certification of satisfactory compliance by the officials of the city, county, or state concerned, and by revoking such permit or lowering grades for repeated violations.[3]

We realize that members of the dairy industry supplying different markets are confronted with a serious problem arising from the variation in laws and regulations in effect in the different states and in the various cities within the states. They are frequently subjected to unnecessary inconveniences and expense of over-lapping requirements and inspections and, in some cases, inability to enter a relative close market. Recently a milk company doing business in one city—selling milk under a grade A label—was forced to go into district court in order to get a permit to sell milk in another city within a thirty mile radius. I believe there is a similar case in our courts at the present time. We believe this practice of cities and small towns limiting the area from which they will accept shipments of dairy products is on the incline. Another common practice is for states and cities to limit the area in which inspections will be made at public expense. Producers outside this area, or distributors who buy from them, must pay all inspection costs. Some cities and states insist upon their own regulations and inspection by their own officials, and many producers and distributors are therefore subjected to inspections by three, four, or even more state, county, or city health departments.

Cities often refuse to accept the inspection reports of other city officials and refuse to enter into reciprocal inspection agreements. That condition was called to my attention recently when one city refused a certification by the health officer of another city. The particular city in question insisted on making its own inspection or an inspection by the State Health Department.

Many more examples could be cited as reasons for the adoption of uniform standards and uniform interpretations of these standards which would make possible mutual acceptance by one area of inspection reports made by another. Of course, there is every justification for ordinances and regulations governing the sanitation of milk supplies and for the proper enforcement of these ordinances and regulations. The record of milk-borne diseases alone is sufficient to justify regulations designed to insure a clean and safe milk supply.

We feel that the best answer to the problem lies in the adoption of the U. S. Public Health Service Milk Ordinance by states and cities. This milk ordinance is accompanied with a code which gives the public health reason for each sanitation requirement and details satisfactory compliance. Voluntary adoption of this milk ordinance has increased from year to year, and by 1946 it was adopted state-wide in three states and as state regulations in twenty-five states.

Briefly, the ordinance defines the sanitation requirements for several grades of raw and pasteurized milk, gives the minimum frequency of inspection and sampling for grading, requires that the grade be shown on the container label, and permits each city to decide at the time of adoption

which grades it will permit to be sold. It provides a choice of two penalties for violation—permit revocation alone or degrading and permit revocation.

Public health departments are not only concerned with the control of milk sanitation, but there is an ever increasing need for control of eating establishment sanitation. This need is also recognized by the industry and by the public. There is a continuous clamor by the public for cleaner food establishments, which is no doubt justified. Again, the USPHS has come forward with the best solution to the question of restaurant sanitation. As a matter of information, it might be advisable to outline the position of the USPHS relative to its service to the states in the field of milk and restaurant sanitation. The USPHS acts solely in an advisory capacity and leaves actual enforcement to the states, except on interstate carriers and even then attempts to get the cooperation of state health department authorities when possible. The program is designed to assist state and local regulatory agencies, which have the necessary legal authority. Its aim is to promote the establishment of effective, well balanced milk and food sanitation programs in each state, to encourage the adoption of effective state and local control legislation, as well as uniform interpretation and strict enforcement through appropriate legal and educational measures.[4]

The public health control of food establishments is necessary from a number of viewpoints, but here again the prevention of food-borne diseases is sufficient in itself. Practically all food-borne diseases are preventable through proper sanitary measures, including, of course, refrigeration. The USPHS Ordinance and Code regulating eating and drinking establishments is available for adoption by states and cities in the same manner as the milk code previously mentioned. The ordinance is offered in two forms in order to give a choice in enforcement—the grading form, which permits enforcement by degrading, or permit revocation, or both, and the nongrading minimum requirements type enforceable by permit revocation only. The non-grading ordinance seems to be more popular than the grading type, particularly with enforcement officials. This is easily understood when we realize that sanitary conditions which would justify an A rating could change within twenty-four hours to justify no more than a D rating.

The responsibility for the enforcement of restaurant sanitation is vested in the health department in thirty-five states, in the agriculture or some other department in eight states, and in both health and agriculture departments in five states. Within the state health department, restaurant sanitation is a function of the engineering or sanitation division in twenty-eight states, of the food and drug division in five states, and of the engineering and some other division jointly in five states.[4]

It is evident that divided responsibility as pointed out above leads to confusion, added expense, and duplication of inspections. These factors definitely interfere with the necessary cooperation of the industry, and such interference makes enforcement problems more complicated.

I am confident that most states are faced with the same general enforcement problems as we have in Texas. These problems briefly outlined are as follows: first, inadequate funds; second, lack of trained personnel; third, food and drug laws which have not been changed to cope with present day conditions. There are other problems, of course, but they can be overcome by a sincere spirit of cooperation between federal, state, and city officials and industry. No law, whether uniform or otherwise, can be effective without the cooperation of those affected.

References

1. Fundamental law of the land, J. Howard McGrath, Food, Drug, Cosmetic Law, 1:3, 1946.
2. Milk supplies and their control in american urban communities of over 1,000 population in 1936, A. W. Fuchs, and L. C. Frank, Public Health Bulletin, No. 245, 1938.
3. Trade barriers in milk industry, A. W. Fuchs, Journal of Milk and Food Technology, 10:4, 1947.
4. Restaurant sanitation program of the united states public health service, A. W. Fuchs, Journal of Milk and Food Technology, 10:1, 1947.

Environment; Its Relationship to Public Health, V. M. Ehlers, Texas State Board of Health, Austin, Tex.:

Until civilized man develops a workable plan that is acceptable to all—a plan that will enable men and nations to live in peace with one another, it behooves us to utilize our resources and

apply our present knowledge in such a way as to make this nation strong physically and economically.

If we are to meet obligations we have assumed and successfully carry out the plans contemplated, medical and sanitary research will have to be vastly accelerated and health knowledge aggressively applied in every section of our nation. Sanitary science has given the health officer a few tools with which to control certain diseases.

WATER: Through treatment of water from surface sources in conventional filtration and chlorinator plants we have been able in our larger cities to reduce dysentery, and typhoid. The addition of fluorine to produce a concentration of 1 ppm. to drinking water appears promising in reducing dental caries. Fluorine is now being added to the water supply at Marshall, Tex., Newburgh, N.Y., Grand Rapids, Mich., Brantford, Ont., Evanston, Ill., Midland, Mich., and Sheboygan, Wis. While hepatitis was found to be water borne, poliomyelitis is still questionable. A good cheap disinfectant for the destruction of amoeba cyst is in the study stage. The use of carbon and chlorine dioxide in water treatment has been found helpful in eliminating certain tastes and odors. The use of the diatomite filter and bursaline are developments that grew out of the recent war and they greatly simplified the treatment of water for the armed forces in the theatre of operations. Algae blooms are being studied to ascertain whether they are responsible for certain intestinal disturbances. Many of our water laws are inadequate. The supplying of safe water to our small communities and rural areas had not kept pace with our municipalities. Cheaper methods for small supplies are needed. Many of our water supplies are supervised by untrained operators. Our water standards are in part arbitrary and our methods of analysis are far from satisfactory. Water consumption has risen and water shortages are prevalent in quite a few localities.

SEWAGE—INDUSTRIAL WASTE: The most common method of sewage treatment in our larger communities is by sedimentation and filtration, or utilization of the activated sludge process. Sedimentation, lagooning and land disposal is practiced in few communities. Irrigation of vegetable crops with raw sewage or sewage effluent is prohibited in some states and frowned upon in others. It is estimated that over two and one half million families in the United States either do not have an adequate water supply or a safe method of sewage disposal. Over a billion dollars in bonds have been voted for water and sewage improvements but thousands of projects are being delayed, due to shortage of materials and no relief appears in prospect. Although great progress has been made in the treatment of domestic sewage, many of our streams are receiving an increasing pollution load. This is due primarily to lack of knowledge in treatment of industrial wastes such as that from rayon, celanese, soybean, chemical, rubber plants, and textile and paper mills. A vast amount of research will be necessary to reclaim our streams. If we are to have sufficient water for our increasing domestic and industrial uses we must learn to re-treat it so that we may be able to re-use our present limited supply of water.

TYPHUS: The encroachment of typhus in the Southern States is being met by well organized rat proofing, poisoning and flea control activities. The placing of 10% DDT dust in rat runs has been found very effective in reducing the flea population on rodents; the use of DDT usually precedes from one to two weeks the placing of poison. Rat-proofing programs are under way in approximately 100 Southern cities. Experience, however, shows that there must be continuous maintenance in order to obtain effective control, and rat-proofing and poisoning should be supplemented by good garbage collection and disposal.

MALARIA CONTROL: Malaria control received quite an impetus during the War Period. Government funds were made available for local areas. New insecticides, of which DDT was the principal one, were developed and malaria has reached its lowest peak in history in Continental U. S. A. One gallon of oil with a small quantity of DDT added will serve the same purpose as 25 gallons of oil as used by the old methods and less labor is required to apply it. This enables municipalities to secure mosquito sanitation within reasonable economic limits. The most outstanding feature of the chemical, DDT, is that the dried crystals in minute quantities cause death when the mosquito rests or walks upon it. Last year the wall of approximately 1 million dwelling units were treated with 5% water emulsion solution in sufficient quantity to leave a residue of 200 mg.DDT/sq. ft. on the wall surface in the malaria areas of continental U. S. A. It is believed that with an expansion of this program malaria may be placed among the diseases of history as has been done with yellow fever.

HOUSING: The relationship between housing and health is rather difficult to define. We do know, however, that crowding is not conductive to good health; and where surveys have been made the common communicable diseases are found more prevalent in the slum areas. Some of the permanent housing units that have been constructed have had mosquito and rat-proofing features incorporated into the design and a good start was made to install correct heating, lighting and ventilation in these demonstration units. Good housing goes further than good health, since it also affects the social fabric of the community. The AFHA Committee on the Hygiene of Housing has made a most worthwhile contribution to the field. Most of our larger cities have a building, or housing code. Some of these are rather antiquated; but at least the importance of the subject was realized by some of the municipal administrators. Shortage of materials and lack of finances still leave our housing situation in a rather chaotic state.

SWIMMING POOLS: Swimming pools are still being incriminated as a source of eye and ear infections as well as of certain respiratory diseases. The modern pool that is being constructed today is equipped to filter and recirculate the pool water. The addition of chlorine in the amount of .2 to .5 ppm is being required in quite a number of our well maintained pools. Athletes' foot (epidermophytosis) still continues to be a problem in some bath houses. A research project conducted by Gotaas is under way by the University of California entitled "Investigation to Determine a Satisfactory Index Organism for Swimming Pools Which Will Show Respiratory Contamination in Tests Suitable for Use in Routine Field Examinations".

FOOD: Considerable progress has been made in recent years by the food industries in the preservation of food. Frozen foods have become more popular partially as a result of the development of economical distribution facilities and improved processing methods. Better sterilization has resulted with the improved types of dish washing machines. New detergents have been placed on the market which facilitate cleansing and sanitary drying operations. For the purpose of reducing food spoilage and retaining original flavors, studies are being undertaken, on temperature, processing time, and packaging. Soil studies are under way to improve the nutritious elements in vegetables and in the grains fed to our milk herds.

HOSPITALS: The Federal Hospital Construction Program has considerable merit. The specifications that have been set up for these institutions, on lighting, heating, ventilation, plumbing and other phases of sanitation involved in structures of this type are in accord with good public health engineering practices. It is most encouraging that greater attention is being given to the designing of nursery units. Even the superintendents of old hospitals have in recent months requested State Health Departments to make recommendations in regard to ventilation and proper air conditioning in nurseries. In the air conditioning of hospital nurseries, it is important to condition the air not only by a germicidal treatment, but by controlling the temperature, humidity, and the velocity of the incoming fresh air. The temperature should be kept year-round at 80 to 85°F. with a relative humidity of 50%. At least 300 cu. ft. of space is recommended per infant and air velocities should not exceed 20 fpm. Filtering and washing the air is important to remove dust and some air-borne organisms, but air entering the nursery should be disinfected also. Ultraviolet radiations will destroy a selective group of organisms and has a place in the air purification field, but it should be installed only under the supervision of qualified specialists.

GARBAGE AND REFUSE DISPOSAL: This phase of municipal house-cleaning has lagged behind in the environmental field. Too many towns in the United States still have no regular collection system, or efficient disposal system. There are still too many open dumps providing fly and rat breeding areas. An effort has been made to manufacture fuel bricketts out of refuse, but the venture has been unsuccessful. Also attempts have been made to convert garbage into a cattle feed and other by-products; but here again, this experiment thus far has not proved economical. Small-time studies have been initiated on garbage grinders and the disposing of the garbage through the water carriage route. It is too early even to make a prediction as to the results of these studies. Perhaps the greatest development has been the inauguration of the sanitary fill. This is a rather elaborate method of burying garbage with a newly developed earth excavating and covering machine. This method has been adopted by a hundred or more cities within the last several years. It has the approval of several State health departments and was used successfully by the Army. The sanitary fill method costs considerably less than the disposal of garbage by incineration.

ILLUMINATION: While the principles involved in lighting have been known to physicists for

some time, it was not until recent years that the public began to realize that the task of seeing was dependent on more than lighting alone. Although the condition of the eye and quantity of light to perform a task are vital, the condition of the surroundings in the visual field must be given equal thought. Since about 85% of all metal impressions are received through the eyes, the importance of illumination, which now includes surroundings, becomes immediately apparent. The surroundings will affect contrast, brightness, glare, diffusion, distribution and the reflectivity of the confining surfaces. Reflectivity brings up color choice, which in turn is governed by the reflection factor desired as well as the psychological associations of the individual and the physiological effect upon him. The Texas State Department of Health has for a number of years been studying this physiologic effect in school children. Correlation has been obtained between such results as fatigue, certain nutritional problems, muscular and skeletal defects and visual errors with illumination, seating, fenestration and other environmental factors. Such studies are still being continued in several elementary schools where data are obtained at periodic intervals. Physical evaluations of the environmental factors for adults are being undertaken by our Industrial Hygiene Section in their plant studies. The results of adverse factors, which can be watched over a period of years, in children are exhibited as variations of child development. In adults, whose skeletal development has stopped, it is exhibited as eye and muscular strain, fatigue, headaches and nervousness with resultant decreased production and morale and increased absenteeism and accident incidence.

INDUSTRIAL HYGIENE: The recent war and the demands made on industry for an increased output of all kinds of materials furnished the impetus for creating industrial hygiene divisions within all of the state departments of health except two—and this demand further filtered to the major industrial municipalities. Studies reveal that absenteeism can be minimized by the application of hygienic principles to the workers' environment. The efforts of the Texas State Department of Health resulted in the passage of the Occupational Disease Compensation Law which, according to some of the industrialists, has reduced accidents, fatigue, eye-strain and absenteeism and has increased the efficiency of the worker. Such developments as atomic power piles, radioactive tracer materials, sterilization by ultra-violet energy and the application of supersonic vibrations in the industrial fields require further research, constant study and continued vigilant control.

AIR POLLUTION: Our knowledge of the effect of contaminated air on the individual is meagre. However, some progress has been made in a few of the larger municipalities on smoke abatement through local ordinances; and recent studies have been made on the disinfection of air in military establishments. The three principal methods for inactivating bacteria and virus that have been investigated are:

a. The use of germicidal mists, or vapors

b. Ultraviolet radiation

c. The application of oil emulsions to floors, blankets and bed linen. The effectiveness of ultraviolet and glycol are both dependent upon the dust that exists. However, the data developed thus far is insufficient upon which to base any definite conclusions other than to say that they have a small measurable influence upon certain respiratory diseases. In the light of our present knowledge, it is imperative that the scope of the present studies be vastly expanded.

Foods, Drugs and the Federal Law, Irvin Kerlan, M.D., Acting Medical Director, Food and Drug Administration, Washington, D.C.:

The Federal Food, Drug and Cosmetic Act of June 1938 has been of inestimable value in protecting the public health and welfare. It has contributed immeasurably to the improvement of the quality and honest labeling and maintenance of the integrity of the nation's foods, drugs, devices and cosmetics, as well as to remove offending products from channels of consumption.

The first and major responsibility of the Food and Drug Administration is the enforcement of the Federal Food, Drug and Cosmetic Act. It is the added responsibility of this organization to enforce four auxiliary statutes; namely, the Tea Act, the Import Milk Act, the Filled Milk Act and the Caustic Poison Act.

It may be helpful in the consideration of the activities of the Food and Drug Administration to recognize that this Federal organization is a relatively small one, whose personnel numbers slightly more than a thousand. More than 650 of these, including the inspection personnel of 234, are trained in various phases of scientific work. The remainder are in administrative, clerical, custodial and other non-professional classifications.

In addition to the administrative personnel most of whom are professional, there are seven technical divisions. The Food Division concerns itself with foods exclusively. It has extensive chemical laboratories and engages in considerable research to acquire technical data for use as a basis for administrative action and to develop new analytical methods for the detection of adulterations. The Cosmetic Division was set up in 1938 to handle problems dealing with the safety and labeling of cosmetics which the Act for the first time placed under Federal control. This division consists of two sections, one for cosmetic analyses and the other for coal tar dye certification. The Act provides specifically that no coal tar dye may be added to a food, drug or cosmetic unless it is from a batch certified by the Food and Drug Administration for such use.

The Division of Pharmacology in its many functions tests drugs requiring bio-assays, such as hormones and related substances, certifies insulin and conducts pharmacologic investigations on acute and chronic toxicity of selected drugs, cosmetics and new substances added to food. The Vitamin Division is engaged primarily in devising and conducting analyses for identification and potency determinations of vitamins by chemcal, biochemical and biological methods, as well as to evaluate claims made for this class of products. The Microbiological Division is concerned with bacteriologic and microscopic examination of foods, drugs and cosmetics for contamination with toxic organisms or filth, for decomposition or for other forms of adulteration.

The division most recently established is the Division of Penicillin Control and Immunology. In 1945 the Act was amended to include the certification of all penicillin and its products prior to distribution in interstate commerce after experimental tests to assure its potency, purity and freedom from toxicity. The Act has been amended to require the same type of certification for streptomycin.

The Medical Division is concerned with the medical phases of those enforcement problems arising in connection with foods, drugs, devices and cosmetics. This group reviews labels to detect false and misleading representations made for the various classes of products as well as to evaluate the adequacy of directions for use and warnings against misuse and the safety of drugs and devices when used as directed. New drugs as defined in the Act are carefully reviewed in the New Drug Section of Medical Division in order to evaluate their safety prior to interstate distribution. The Chemical Section attached to this Division conducts special chemical analyses of an experimental nature, which require special techniques and research. The Medical Veterinary Section of this Division deals with the entire field of foods, drugs and devices represented for use by animals.

The annual appropriation granted to this Administration to carry out its manifold and diverse services is about four and a quarter million dollars. This represents an annual per capita cost of three cents, a markedly inexpensive protection service for the American public.

The Federal Food, Drug and Cosmetic Act includes among its prohibited acts the introduction or delivery for introduction into interstate commerce of any food, drug, device or cosmetic that is adulterated or misbranded; the adulteration or misbranding of any food, drug, device or cosmetic in interstate commerce; and the receipt in interstate commerce of any food, drug, device or cosmetic that is adulterated or misbranded, and the delivery or proffered delivery thereof for pay or otherwise. Violative goods shipped in interstate commerce may be seized and the shipper may be prosecuted criminally and enjoined from further violations. These enforcement procedures are brought in the Federal courts. In the case of seizure, the owner of the seized goods may allow them to go by default which results in either destruction or diversion to legal uses under court order; he may elect to admit the violation and ask the court to permit the withdrawal of the goods under bond for relabeling or other action which brings them into compliance; or he may deny that the goods are in violation and elect to go to trial. In the case of criminal prosecution or injunction proceedings, unless the defendant admits guilt, the case is scheduled for trial.

In the presentation of court cases involving pediatric questions, the Government relies upon the assistance of outstanding and recognized experts in this special field to explain to the court and jury the medical basis for the charges from the pediatrician's standpoint. It cannot be stressed too forcefully that it is only with full cooperation of pediatricians that the Food and Drug Administration is able to bring about effective corrections in the labelings of the various classes of commodities referred to, in the interest of the public welfare, and more particularly children.

In an effort to obtain the pediatric consensus with respect to the truthfulness or adequacy of labelings for food and drugs, as well as to assist in the solution of some of the many problems

arising in that connection, this Administration has received recently the cooperative assistance of the American Academy of Pediatrics through a special Committee created by it to work with the Food and Drug Administration. It is anticipated that this arrangement will bring about the ready exchange of information beneficial to both groups, who are concerned equally with the health and welfare of children.

Foods are generally accepted as being fit for human consumption by the mere fact that they are held out for sale. It is only through study of the food sections of the Act that it becomes apparent that there are many types of adulterations and misbrandings of foods which are prescribed. The significance of such violations of course depends wholly on the nature and extent of the infraction. It should be pointed out that legal actions against violative foods represent a major part of the enforcement program of the Food and Drug Administration. The nature and seriousness of these actions can be recognized readily by their review.

Food adulterations involving health are first in order of significance and these are of varied character. Under the terms of the Act the addition of poisonous and deleterious substances to food is prohibited unless such substances are necessary for production or cannot be avoided in good manufacturing practice, in which case provision is made for the establishment of safe tolerances by regulation. The practice of using poisonous preservatives to check decomposition which could be avoided by adequate plant sanitation is a violation of this provision which has been condemned unqualifiedly by the courts.

In its regulatory program directed against injurious preservatives and the foods containing them, the Food and Drug Administration became concerned with an epidemic of vomiting and diarrhea which was occasioned by the drinking of an orange-type beverage found upon investigation to contain the deleterious preservative monochloracetic acid. With the cooperation of state and local officials an immediate roundup of the nationally distributed beverage base used in preparing this drink was undertaken. The quantity of concentrate sold, according to the firm, produced over 65 million bottles of orange beverage. A criminal information based on shipments to which the illnesses were traced was terminated with a plea of guilty and a fine of $5,000.00.

Other foods seized because of the presence of monochloracetic acid included pancake sirups, chocolate flavoring sirups, salads dressings, fruit-type beverages, and chow-chow relish. Within the past year the use of these deleterious substances has been diverted largely to alcoholic beverages, particularly light sweet wines. In the fiscal year 1947, 152 shipments of wine and beer containing toxic preservatives were seized.

Fruits bearing spray residues used as insecticides and containing arsenic, fluorine, lead, or DDT in excess of announced safe tolerances are adulterated under the terms of the Act and subject to action. Since spray residue removal is sometimes undertaken when apples are removed from storage just prior to shipment, regulatory surveillance is required throughout the year rather than only during the harvesting season.

The use of mineral oil in food represents an outstanding example of the deleterious effect on public health of current economic developments. The scarcity of vegetable oil through the war years brought a widespread attempt to substitute mineral oil for food oil in a variety of foods, including popcorn, mayonnaise and salad dressings, salad oils and oil seasonings, candy bars, potato chips and toasted peanuts. Substitutions of mineral oil for food oils has resulted in numerous legal actions, several of which were tried in the Federal courts. Based on recent scientific investigations showing that mineral oil interferes with the absorption of the fat soluble vitamins A, D and K, the courts have stated specifically that mineral oil in food is a deleterious substance which renders the food injurious to health. One manufacturer was enjoined by the Federal court for making interstate shipments of popcorn containing mineral oil. This concern had shipped popped corn containing as much as a full therapeutic dose in a single consumer-size bag.

Other dangerous ingredients which have been found in foods include glass particles and slivers from defective or carelessly handled bottles of imported whiskies, brandies, wines and other liquors. This brought a serious import control problem about three years ago, when 70% of the lots offered for entry had to be detained for filtering before entry was permitted. The relative decrease in the number of detentions of such imports indicates a fundamental correction in the foreign production centers. Glass slivers were also found last year in three domestic lots of ground coffee, being salvaged despite knowledge that they contained glass. They were promptly seized.

The presence of a high lead content in maple sugar and sirup, introduced by gathering the maple sap in lead-painted buckets, is representative of another health hazard which is corrected under the provisions of the Act.

Foods containing other dangerous or nonnutritive substances, as exemplified by the presence of pit splinters in pitted prunes, and stones and burrs in dried peas or beans, and the accidental substitution of borax for salt in canned peas, are likewise seized as adulterated foods, and require constant vigilance and inspection for detection. By this provision of the Act, candy containing foreign bodies such as toys has been eliminated as contraband and children are protected against unnecessary injury.

Sea foods of themselves represent a major enforcement problem. To prepare an acceptable pack of an article so perishable and so subject to contamination requires constant vigilance of the plant management. Fecal pollution in crab meat is responsible for numerous seizures and several criminal prosecution actions each year. Severe poisonings often followed by death have been caused by the eating of clams and mussels which have acquired poisonous properties through contamination with small plankton organisms which inhabit certain coastal waters seasonally. In the case of shrimp canning, the canner may request supervision by a Food and Drug Inspector during the packing season. The sea food packers also may obtain assistance of the Food and Drug Administration for oyster packing, providing a prescribed sanitary code is fulfilled. Packers of other varieties of sea food have not applied for this service.

Food poisoning outbreaks usually originate in the kitchen where the food is prepared for the table but occasionally they are traced to foods of interstate origin. The Food and Drug Administration investigates all reported outbreaks promptly so that the offending food can be identified and located, and if interstate shipments are involved remaining lots can be removed from the market in time to avert further injury to consumers.

Tremendous losses of food that becomes filthy and decomposed through failure to protect it from rodents and insects can be prevented by correction of insanitary conditions. It is encouraging to report that organized industry is making basic corrections of conditions and practices to protect the food. Under the leadership of their trade associations, several large industries have set up organizations to deal with sanitation on an industry-wide basis; as yet however, regulatory attention to filth and docomposition cannot be relaxed.

The courts are not disposed to countenance the shipment of filthy food, insanitary factories or practices, or failure to protect sound food through storage negligence. In line with its practices for the past 40 years, the Food and Drug Administration made a seizure of a shipment of macaroni which became contaminated while stored in a rodent-and-insect-infested warehouse where it was placed after its interstate journey. Section 304(a) of the Act provides in part that articles which are "adulterated or misbranded when introduced into or while in interstate commerce . . . shall be liable to be proceeded against while in interstate commerce, or at any time thereafter, on libel of information and condemned in any district court of the United States within the jurisdiction of which the article is found . . . ." The District Court for the District of Arizona dismissed the libel in this Phelps Dodge case after holding that the defiled food was not adulterated "while in interstate commerce." The District Court of Appeals for the Ninth Circuit affirmed the decision and the Department of Justice petitioned the Supreme Court for a writ of certiorari. The writ was denied.

These court decisions are interpreted by the Food and Drug Administration to mean that as far as contamination is concerned the interstate commerce journey of the goods ends when they come to rest at the consignee's warehouse. The decisions thus end an important protective public service to the ultimate consumer that has been carried out for over forty years under the present law and the original Food and Drugs Act of 1906.

Until the Phelps Dodge decision was handed down thousands of shipments of foods and drugs that became filthy, debased or deteriorated after interstate transportation were seized and condemned under this provision and thereby were prevented from reaching the consuming public. The authority to make seizures in such circumstances was never challenged by court contest.

As is readily apparent is may not be possible to prove that contamination or deterioration occurred before the interstate journey ended, and for this reason the Phelps Dodge decision places an *impossible* handicap on effective enforcement to protect the health and welfare of the public. It is difficult to visualize the magnitude of the breach in consumer protection that has occurred.

Actions to remove filthy and decomposed foods from the market involved nearly 70% of all food seizures in 1946. In number, there were 1,713 seizure actions in the fiscal year. Included among the classes of products receiving regulatory attention were more than 8½ million pounds of cereal products such as flour, corn meal, brewers grits, and popcorn seized as unfit for human use; confectionery; dairy products and eggs; fruits and vegetables; seafood; nuts and nut products, and a variety of unrelated filthy and decomposed food products. These decisions immediately stopped terminal seizures for the remainder of the fiscal year 1947 and the percentage of food seizures on filth charges dropped from 70% to 53%.

The Food and Drug Administration has brought this legal decision to the attention of Congress and has pointed out the public welfare need for amendment of the Act in order to safeguard the American public from adulterated and misbranded food while being held for sale after interstate transportation. The House Committee on Interstate and Foreign Commerce has approved an appropriate amendment, which is now pending on the calendar of the House of Representatives. With the recommended amendment of the Act it is felt that it will simply restore a situation thought to exist before the Phelps Dodge decision. State food and drug officials have endorsed the amendment, confident that it will not disturb the scheme of cooperation between the Federal and state officials. It should be recognized that the needs of consumer protection have not been met adequately even by combined Federal and local forces.

Special labeling requirements are set forth in the Act to cover foods which are represented for special dietary uses. Among such dietary foods, depending on their ingredients and character, are foods for infants and children. Labels for special dietary foods must bear the information concerning their vitamin, mineral and other dietary properties as has been determined and set forth in the regulations under this section of the Act, in order fully to inform purchasers as to their value for such uses. In the case of vitamins and minerals the quantity of vitamin or mineral supplied in a specified quantity of such food should be accurately stated on the label. Infant foods are required to bear on the label if the product is fabricated from two or more ingredients, the common or usual name of each ingredient including spice, flavoring and coloring. Additional information on the label is required if the food simulates mother's milk or serves as a partial or complete substitute for human milk.

The salient requirements of the Act with respect to adulterations and misbrandings of foods are paralleled with respect to drugs and devices. These commodities must meet the following provisions of the Act:

1. The article must conform with the strength, purity or quality which it purports or is represented to possess.

2. The labeling (this includes all printed and graphic matter which accompanies the article) must be truthful. Extravagant therapeutic representations made for an article constitute a major problem under this section of the Federal Food, Drug and Cosmetic Act.

3. The label must bear the name and address of the manufacturer, packer, or distributor, as well as a statement of the quantity of contents. In this connection a note of warning should be stressed that the vendor of drugs should be known to be reliable to the physician user, prior to the purchase of drugs. Recently the Administration had called to its attention an unfortunate circumstance in the Northwest. A fly-by-night salesman doing business under the name of Associated Allergaton Laboratories, purportedly of 421 Moss Avenue, Oakland, Calif., but sometimes labeled as coming from a fictitious Chicago address, sold directly to physicians ampuls of a product called "Allergaton" which is represented as a specific for skin irritations such as itching, for allergic disorders and arthritis. Analysis of samples of this product revealed that it is an alkaline polysulfide solution which causes severe reactions when administered by injection to patients. The Food and Drug Administration after a long search located the responsible person and found there is no firm such as Associated Allergaton Laboratories of Oakland. The man was manufacturing the product in his hotel bedroom by dissolving liver of sulfur in ordinary tap water. With the aid of the state authorities this drug peddler was apprehended and was assessed a heavy fine by the county court, which he will probably have to work out in jail for several years, since he is reported unable to pay it.

4. The labeling must bear adequate directions for use. In the case of articles sold for lay use proper indications for administration must appear and adequate directions for such indications must be supplied. Articles which can be used safely or efficaciously only under the supervision of physicians, dentists or veterinarians must bear the statement: "Caution: To be dispensed only by

or on the prescription of a physician, dentist or veterinarian" in lieu of directions for use, provided the other requirements of the regulations under this section of the Act are met. For products distributed under this special exemption, the manufacturer generally supplies directly to the physician, upon request, an informative brochure apart from the market package which sets forth detailed scientific and technical information relating to the use of the drug or device. In the case of new drugs such descriptive circulars are required to be submitted for critical review before distribution, inasmuch as the practitioner may not be sufficiently well acquainted with a new drug to use it both safely and efficaciously if he does not have carefully prepared information available.

A special class is made of drugs packaged in ampuls or cartridges to be administered by injection under medical supervision. In this instance adequate directions should accompany the product.

5. The labeling must bear adequate warnings against unsafe use in those pathologic conditions or by children where its use may be dangerous to health or against unsafe dosage or methods or duration of administration or application in such manner and form as are necessary for the protection of users. In this instance Congress required specifically that the labelings for drugs bear such warnings as are necessary for their safe use by children. In that connection, based on fairly recent reports in the literature, the Food and Drug Administration has recommended that the labeling for calcium salts for injection clearly display the warning that the drug should not be injected intramuscularly in children. In order to extend this protection, it would be extremely helpful to have made available to the Administration reports of injury which arise in connection with the use of drugs generally. The Federal Food, Drug and Cosmetic Act does not require reporting of drug injuries; however voluntary submission of such information to this Administration as an isolated report will be valuable since other physicians may have had similar experiences and the aggregate of such findings may lead to significant and worthy conclusions.

6. The article must not be dangerous to health when used in the dosage or with the frequency or duration prescribed, recommended or suggested in the labeling thereof.

7. In the case of certain drugs intended for use by man, if they contain any of a list of narcotic or hypnotic substances which have been found to be habit forming, or any derivative of such substance, the label must bear the statement: "Warning—May be habit forming" in juxtaposition to the quantitative declaration of the drug. Such drugs include, among others: barbiturates, chloral, cocaine, codeine, morphine, opium and paraldehyde.

8. The label of non-official drugs must bear the common or usual name of each active ingredient including the quantity, kind and proportion of any alcohol, and also including, whether active or not, the name and quantity or proportion of any bromides, ether, chloroform, acetanilid, acetphenetidin, amidopyrine, antipyrine, atropine, hyoscyamine, arsenic, digitalis, digitalis glucosides, mercury, ouabain, strophanthin, strychnine, thyrod or any derivative or preparation of any such substances contained therein. Non-official drugs sold for prescription use only must bear a quantitative declaration of each active ingredient so that the professional user can evaluate the product with full information as to its composition.

Drugs which become adulterated represent frequently articles of major health significance in view of the dangerous effects that may arise from administration of a potent drug which may be contaminated or substituted in whole or in part by another potent substance. Errors of compounding of drugs may result in fatal outcomes, unless apprehended and the offending articles removed from interstate channels. Several recent representative instances of major drug adulterations resulting from compounding errors and subsequent failure to test finished batches before distribution included digitalis tablets of nearly three times the declared potency, an obesity treatment containing 11 times the declared amount of atropine sulfate in some tablets, another drug with 6 times the labeled amount of phenobarbital, and another in which 6 pounds of pilocarpine hydrochloride had been used instead of the 6 ounces the formula required. Label mix-ups resulted in two instances of packages labeled as vitamin B complex solution but which contained an oil solution of estrogens. Each was in a type of container such that the physician could not have noted the substitution before administering the drug by intravenous injection, as directed on the label, a procedure that would almost certainly have caused fatal results. Fortunately early sampling and analysis led to seizure and recall of the offending goods. As in other cases of drug mix-ups, the substitutions were accidental but they are indicative of the carelessness in the handling of an article that may cause irreparable damage if an error is permitted to occur.

Economic-type violations have been found particularly in the field of estrogenic hormones. In

one instance, the manufacturer was substituting diethylstilbestrol for the natural estrogenic hormones, and shipping the product under counterfeit labels.

Non-sterility or the presence of undissolved particles in drugs for injection represent a type of adulteration which is penalized severely by the courts. Subpotent drugs also may represent a serious violation with major health importance. Exemplary of this type of adulteration is subpotent pituitary or epinephrine preparations which are inherently dangerous since physicians would fail to attain the desired physiologic effects in administering them to patients.

With respect to misbranded drugs because of flagrant and unwarranted claims the general survey of stocks of proprietary remedies has resulted in detection of fewer violations since this type of misbranding has been actively singled out for correction. Those who attempt to misrepresent their products tend to use more devious types of labeling, such as circulars which may be stored in separate packages until they are brought together with the medicine on the dealer's counters ultimately, or oral promotion in a modern counter part of the old-time medicine show.

Irrespective of how the misbranding arises, the attempt to mislead users in order to sell nostrums continues as a reprehensible practice which requires legal action for correction. No infrequently the persons responsible for the misbrandings elect court presentation to maintain the position set forth in the labeling. In such instances the Government must rely on the services of experts to present the clinical, scientific and technical data to establish the falsity or misleading character of the statements so charged.

In the field of pediatrics, consideration must be given to clarification of several specific problems and practices which serve as a basis for misleading representations. As an example of one of the fundamental determinations to be made is the place of medicated oils in the nursery for prevention of skin infections. Evidence generally recognized establishes the lack of value of this practice and reliance on it as misleading to users, yet endorsements of this practice by hospital attendants continue. Another fundamental need is to set up definite drug dosages for children of various weights or ages. Too often drug dosages for children appear to be set up empirically without pharmacological evaluation of the proper dosage in particular disease conditions. More recent pharmacological developments have begun to take cognizance of this lack and before introduction of a few new drugs, the product has actually been administered to children to study its effects at various dosage levels. This is a necessary practice which should be continued and extended generally. Other urgent problems of similar character have been presented to the Academy's Committee to Cooperate with the Food and Drug Administration for consideration and comment in an effort to obtain the pediatric consensus.

From a public health standpoint, the inclusion of the new drug section of the Act represented Congressional recognition of a constructive and valuable contribution to the safe use of drugs, whether to be administered under medical supervision or used generally. Legally no new drug can be introduced into interstate commerce unless an application filed with the Administrator of the Federal Security Agency establishes the safety of the drug in the conditions for which it is recommended or suggested and has become effective.

In the first nine years of operations under this provision of the Act 6,265 new drug applications were submitted. Of these applications, 4,162 have been permitted to become effective, approximately 1,279 were incomplete, 400 were not new drugs, and 376 were withdrawn voluntarily by the applicants. The remaining applications are either under consideration at the present time or orders have been issued refusing to permit them to become effective. Of primary concern in consideration of a new drug from a medical standpoint is the adequacy and suitability of the full reports of investigations both clinical and experimental to determine the safety of the drug. The Food and Drug Administration cannot undertake to outline the nature and amount of investigational work which may be required to establish the safety of a new drug, as such studies will depend of necessity upon the nature of the drug and facts developed during the preliminary investigations. In a general way, an attempt to outline the laboratory and clinical studies that may be necessary for the evaluation of the safety of certain new drugs is set out in the *Journal of the American Medical Association* for December 9, 1944. In that connection it should be pointed out that the submission of a few well conducted studies will greatly outweigh voluminous reports of uncontrolled investigations.

With the enactment of the Act in 1938, devices came under Federal supervision for the first time. The violations which have been encountered are of a serious character. Unscrupulous adventurers in the business of furnishing cure-all therapeutic devices are rampant. They victimize people who can ill afford the excessive prices of these contraptions. One device selling for $365.00 was

advertised by a circular claiming that 52% of its purchasers had an annual income of under $3,000.00. It has seemed that the persistence of these offenders is directly proportional to the increasing absurdity of the claims they make for their gadgets. Even more tragic is the fact that persons turn to these fraudulent devices for the treatment of serious diseases which require immediate competent diagnosis and rational treatment.

A vapor-bath system, consisting of certain drugs and plumbing connections between a generator and bath cabinets, which could be purchased for $2,200.00, was represented as effective for diabetes, abscess of the lungs, decay of the jawbones, and blood poisoning, among a long list of other ailments.

An apparatus for administering electric shock, selling for $1,200.00, was represented for abscess of the liver, internal growth, heart disease, paralysis, cancer, tuberculosis, infantile paralysis, and other disease conditions.

A device for administering an enema, priced at $1,190.00, was offered for the treatment of arthritis, rheumatism, neuritis, high and low blood pressure, toxic heart conditions, ulcers of stomach and bowels, colitis, chronic appendicitis, gall bladder and liver troubles, kidney and bladder troubles, asthma, migraine, toxic skin troubles, lumbago, and for good measure, "a host of ills that have heretofore been obscure."

Another device called "Spectro-Chrome" is a 1000-watt lamp in a cabinet supplied with different-colored glasses to fit an aperture through which the light bathes the patient. With head pointing toward the north, the patient receives "tonations" at favorable times of the day, with a "Favorscope" supplied to correct for "solar, lunar, terrestrial radiant, and gravitational influences" based on "vibrant breath phenomena" as adapted from yoga. By using appropriate glasses to color the light is required for the particular disease to be treated, the device was claimed to be effective for diabetes, cancer, tuberculosis, syphilis, and a long list of other ailments. Dinshah P. Ghadiali, who manufactured the apparatus and who scorns the use of drugs said: "Give me a case of appendicitis, and I will send the man back in one night, having his appendix inside him instead of in a glass bottle and $300.00 out."

This lamp, more marvelous than Alladin's, was not for sale. To get it, one had to join an "institute" at a fee of $90.00. The lamp was then furnished free. We know that at least 5,000 were distributed—Ghadiali, himself, claimed the figure was 9,000. With them, for a price, was distributed so-called "enclopedias" and other "literature" which gave voluminous information about the use of the lamp and sought to cloak the scheme in Oriental mysticism and sanctity.

The first action against the lamp was a simple seizure. After a trial which lasted 30 days, the jury rendered a verdict for the Government. The Court was so incensed at the abuse of public welfare that he supplemented the decree condemning the lamp with an injunction against its further distribution. Ghadiali nevertheless continued to distribute it. A campaign of multiple seizures followed, which did not stop him. Then criminal prosecution was filed against Ghadiali and his corporation. During the trial, which last 42 days, the Government presented an array of physicians and relatives of victims who had used the device and died from the diseases it was represented to cure. Speaking from the witness stand, the son of a man who had died from diabetes said to Ghadiali: "You told my father to stop insulin! You said for him to eat plenty of brown sugar and starches! You said he would recover with Spectro-Chrome!" The jury brought in a verdict of guilty and the court imposed against Ghadiali and his corporation a fine of $20,000.00, and a 3-year prison sentence against Ghadiali, but imprisonment was suspended on the condition that the business be stopped. Sentence was deferred on four of the counts against Ghadiali upon the same condition so that, if he resumes business, he faces the possibility of a prison sentence of seven years, and an additional fine. He has appealed this decision and the case will be reviewed in the fall term of court by a circuit court of appeals.

Foods, drugs, devices and cosmetics which are offered for import into the United States must comply with United States requirements for domestic shipments. They are refused admission if it appears that the article has been manufactured, processed or packed under insanitary conditions, if the article is forbidden or restricted in sale in the country in which it was produced or from which it was exported, or is a new drug as recognized under the terms of the Act.

Although the vast majority of persons and firms subject to the provisions of the Act seek to abide by it, the difficulties and complexities inherent in the manufacture and labeling of many worthy and valuable products make it understandable that unintential violations sometimes occur. Most of

the violations by honest and well-intentioned manufacturers arise from inadvertence, accident, or thoughtlessness. A high degree of care and precaution is necessary if violations are to be avoided entirely. That is as it should be because those who supply the nation with such vital necessities as foods and drugs assume a role of unusual responsibility for the integrity of the composition and truthfulness of the labelings for their products.

The pediatrician as a consumer is directly benefited by these regulatory activities; as a participant in these activities he assists in the development of enforcement programs and in putting them into effect.

It should be repeated that protection of the consumer from misbranded foods, drugs, devices and cosmetics is the purpose of the Federal Food, Drug and Cosmetic Act. The Food and Drug Administration through its limited staff maintains vigilance over these various classes of commodities to provide this protection. With the public-spirited cooperation of the experts in the field of pediatrics a wider area of protection can be provided in the interest of the health of children.

ROUND TABLE DISCUSSION

BEHAVIOR PROBLEMS OF INFANCY AND EARLY CHILDHOOD

ARNOLD GESELL, M.D., *Chairman,* AND CATHERINE S. AMATRUDA, M.D.

Chairman Gesell: Custom has it that the Chairman should launch the discussion with an introductory statement. I shall be brief because behavior problems are numerous enough. Besides we propose to divide this session into two parts. At the end of the first half, Dr. Amatruda, who has had an incomparably rich experience with all sorts of infants and children, will make a statement introducing the subject of developmental defects and deviations. Although we shall touch upon a wide variety of problems during the morning, we shall probably not wander very far from the central theme of growth and development.

All children, whether normal, subnormal, atypical, or superior are confronted with the universal problem of development—of growing up. The most serious behavior problems are those which interfere with optimal development, taking as a base line the natural growth potentials of the child. Many problems may seem serious and may be very troublesome, without greatly harming the child's fundamental welfare. The degree of troublesomeness often depends upon the attitude of the parents. This business of growing up applies to the parent as well as the child. She (or he!) may not take a mature grown-up attitude toward the child's conduct. The problem is thereby aggravated or even created. Change the attitude and the problem evaporates—disappears in thin air. In our discussion we shall have to reckon with the parent-child relationship as a clinical reality, as a bundle of symptoms which register the actual state of affairs. Problems cannot always be solved by direct frontal attack. They must be approached peripherally via the parents' psychology. The most magic cures which the pediatrician can effect in the field of behavior disorders may be achieved by altering the parents' philosophy.

Every parent has a philosophy of child care. It may not be formulated in words, but it expresses itself in actions, attitudes, in alibis, in questions, in misgivings, in protests. Even before the child is born the expectant mother may reveal her general outlook, and may profit from a hint or two by way of psychologic orientation to the tasks of parenthood which lie ahead. In fact, this Round Table might give brief consideration to the possibility of prenatal guidance in the primipara, assuming the aid and acquiescence of the obstetrician. We might also inquire whether the rooming-in arrangement at the hospital has value or disadvantages for the psychologic orientation of the parents during the neonatal period. At any rate, as the child grows up these parents are likely to illustrate more or less consistently one of three brands of philosophy: 1) authoritarian; 2) laissez-faire; 3) developmental:

The authoritarian approach takes its cue from absolute standards of right and wrong. It believes in strict discipline, possibly even in corporal punishment. It holds the child to the mark. It has considerable faith in habit training and in rigid schedules.

Laissez-faire doctrine doesn't worry about absolutes at all. It does not constrain the child. It has faith in non-interference. Things will work out for the best if you let them alone.

A developmental philosophy lies between these two extremes. It looks with some skepticism on rigid absolutes, and it does not favor license. It believes in guidance based on a knowledge of the ways of growth. When a pediatrician looks at discipline, he will be inclined to take a first look at the child's stage of maturity. He will not make an objective of discipline for its own sake, realizing that even in a child the discipline which really counts is self discipline. The child must do his own growing.

I should like to ask whether management is not a better concept than discipline—externally imposed discipline.

These philosophic issues all come to a head in relation to that disgraceful everyday problem which is opprobriously labelled disobedience! It is very unwise to make a fetish of children.

The philosophy which leaves the most room for a sense of humor, for sympathy, and for

From the Annual Meeting, Dallas, Tex., December 8-11, 1947.

mutual adjustment is a developmental philosophy, which is sensitive to the ways of growth. All aspects of the child's behavior are subject to inescapable laws of development—his sleep, feeding and activity rhythms, his motor coordinations, his crying and language, his social reactions, his table manners and even his morals. For this reason every behavior problem should be projected against a developmental frame of reference. Fortunately, there are very few behavior problems which are not in history and essence a variation or a deflection of normal mechanisms. Both benign and serious behavior deviations demand interpretation and treatment in terms of the mechanics of development.

This is one reason why self-regulation with respect to infant feeding schedules has come up for consideration in recent years. The new trend in pediatrics is away from authoritarianism to individualization. Is it possible that ironclad schedules rigidly imposed in accordance with clock-time may sometimes be harmful? The infant is in such close league with nature that he knows a great deal about certain fundamentals: when to eat; what to eat; when to sleep; when to wake up; when to be sociable; when to play alone; when to obey; when to resist. The culture must, of course, guide and direct, but it cannot overlook the innate wisdom of the body which is also the wisdom of the baby's mind. Whatever the practical difficulties may be in putting a self-regulation program into operation, the merits of the case can be decided only on the basis of the developmental welfare of the infant.

Fathers need the developmental point of view just as much as mothers do. For example, some of them think that a child should obey promptly, the very moment he is spoken to. They speak in a commanding voice, and they are irked by lack of compliance, and feel that they lose face (especially if there is company in the house). This surely is not an enlightened or enlightening attitude.

Fathers are often too strict about the child's toilet habits. They think that once a fair degree of competence is gained, the job is done and there should be no backsliding. This is altogether contrary to the laws and mechanisms of development.

Fathers who have glowing ideals of physical health, athletic vigor and sportsmanship, are sometimes likely to bear down too heavily on a child of tender age. They are too annoyed by finger sucking and other tensional habits; they are chagrined when their two and one-half year old shows an "effeminate" interest in dolls and domestic activities; they are too severe when their fine grained seven year old fails to fight back on the playground. They are much too eager to make a man of him in a hurry.

Fathers can be too sensitive as to what other people think of their child. They may feel that every bad form of behavior which occurs is in danger of becoming permanent. They are too gloomy when a four year old tells tall tales and brags shamelessly.

These are the apparently trivial behavior problems which arise in the everyday life of the family. We do not wish to suggest that the problems are very important in themselves. What is important is the general temper of the home, and its atmosphere from day to day.

Here lies the supreme, over-all value of a developmental philosophy of child care. The old fashioned type of father (and he may even be a young veteran from the last war) thinks too much in terms of the present and of absolutes. The more modern father likes to know what makes the child tick. He has a feel for the construction and operation of machines—carburetors, batteries, and radio tubes. This gives him a certain respect for the machinery of behavior and the mechanics of development, because a child after all is an extremely complex action system, which must be handled with care rather than with harshness.

This technologic type of father may be very susceptible to a developmental philosophy. A five minute talk by the doctor can readily give him his bearings. He does not demand a rule of thumb. What he wants is orientation. And the doctrine of development can give him just that.

To sum up, a developmental philosophy of child management has these four advantages:

1. It gives orientation. It gives general principles which apply to all kinds of behavior problems.

2. It enables the parent to anticipate what is likely to happen at a given stage. A degree of disequilibrium is expected at the two and one-half year age level. It is comforting to know that a stage of relative equilibrium is in the offing at three years.

3. Developmentalism leads to a better appreciation of the child's difficulties. His permanent behavior problem is the problem of growing up. The concept of growth makes it more possible to understand the factors which are at work in the child's malbehavior. It distinguishes between the petty and the really important factors of mental health.

4. A developmental philosophy enables parent and doctor to see the cycle of psychologic growth in perspective. This favors faith, sympathy, and a sense of humor. Perhaps it is possible to enjoy most children despite their interesting behavior problems.

Dr. George D. Johnson—Spartanburg, S.C.: Suppose a two and one-half year old child, playing in the front yard, runs into the street in front of a truck. How is the best way to impress on that child that he shouldn't go out in the street? I must have done the wrong thing when I "switched" my boy, but he's been very leary of running into the street ever since.

Chairman Gesell: Well, the proof of the pudding is in the results. On the other hand possibly we would avoid generalization on the basis of a critical and emergency type of situation. Most of the problems of every day child life do not have an emergency aspect and if we draw a general conclusion from one example, go all out for corporal punishment, and say, "See, what a fine thing it is." Well, that doesn't get us anywhere either. We can understand this impulsive protection on the part of the parent but under these conditions if it's done without "flogging"—so much the better.

Dr. B. B. Breese, Jr.—Rochester, N.Y.: Is corporal punishment advisable in the age group around two and one-half to three years in trying to teach a child to recognize a dangerous act. Such behavior as turning on the gas, pulling things over, getting near water or streams, going out in the street, a child may not understand is likely to do him bodily harm. I see no logical way of approaching a solution except by the method of corporal punishment.

Chairman Gesell: My answer would be very much the same. If it's a question of ash-trays on the end table, then perhaps they ought to be moved instead of making an issue out of it by putting an ash tray at the edge of the table and then punishing the child every time he snatches it. If we get too logical about any of these matters we always get into absurdities and in the case of ash trays, I'd put them up so high that the child couldn't get them. If you've got a very active, run-about child, maybe the important thing is to have a type of room where he will not be stumbling into these problems. We have 75 to 80 children in attendance each week in a child guidance nursery ranging from 1½ to 4 years and let me assure you they are high spirited children, with a staff of competent workers and with that complex environment of the guidance nursery. We manage the children and environment in such a way that we do not have to use corporal punishment. And, that doesn't mean we let them do everything they want to.

Dr. J. W. Bruce—Louisville, Ky.: What practical methods concerning discipline would you use in the home?

Dr. Amatruda: Between the ages of 15 months or so to 3 or 3½ years, when children are so apt to exploit dangerous situations, it is safer to eliminate hazards than to rely on parental vigilance and authority, and on punitive measures after the hazard has been sampled. We advocate fences, gates, safety devices on windows, putting matches, medicines and poisons out of reach; if necessary the handles can be removed from the gas stove. Such measures may be awkward for the parent, but they are safe and effective. In the meantime an attitude of cooperation and conformity is being built up in the child, he gradually and responsibly accepts a few rules and limitations, and one "dangerous age" is past. Each age, of course, has it's own dangers.

You can get obedience, yes, in a specific situation for which you have punished. Quite aside from any theories of child guidance and child training, there are two very practical objections: first, you have to permit the child to expose himself to danger before you can punish and second, there is no carry-over to another hazard. Life then becomes a series of emergency situations, and a series of punishments.

The parent has ample opportunity to assert his authority when the child approaches a hazard, by removing the child bodily from the situation; this is a deprivation of freedom of action and is, in that sense, a punishment in itself. Interest the child in something else, then go back and remove the hazard.

Dr. C. A. Erickson—Pasadena: About what age do you expect cooperation in these matters from a child?

Chairman Gesell: That cannot be answered in terms of an absolute age. We get cooperation in dressing from the one year old child when he puts out his arm for a sleeve or his foot for the shoe. He's mature enough to do that. We get cooperation in the nursery when lunch time comes and graham crackers have to be passed. We get one kind of cooperation from the two year old child and another from the three year old child, who does it better than the two year old. A few weeks

ago, I saw the behavior of a two and one-half year old child when we had a blind boy, aged three in the clinic. The nursery group assimiliated this blind boy very nicely. They stared at him a little bit but presently when they went out to the play yard on the slide, little Barbara, two and one-half years old became his manager and cooperative assistant. When he was at the bottom of the slide she would put out her hand and lead him to the bottom of the ladder, then he would climb up and slide down and she'd lead him back again. So, the answer to your question is, that the cooperation must be graded to the maturity of the child's behavior equipment at that particular time and within the limits of his maturity you should expect a certain degree of cooperation. But you cannot set up cooperation in the abstract as an ideal. Even our nursery school is a little in danger of overstressing cooperation. I like to see a child who's a bit independent and, because of a self reliant temperament, goes into a corner and plays by himself in his own particular way. Maybe that child is going to be a very fine citizen. I'd like to answer the question more simply but the developmental point of view obliges us always to think in terms of the maturity level and of specific patterns of the age group and negatively the developmental approach obliges us not to solve our problems in terms of absolute generalizations. After all, we must take a different point of view with regard to the lying of a four year old child and the lying of a ten year old child.

Dr. O. E. Barbour—Peoria, Ill.: At what age of the child should we warn parents about thumb or finger sucking?

Chairman Gesell: About 16 weeks of age when they may expect to see it. I would explain that at that time, for maturity reasons, the hands come to the mouth naturally and that the sucking is secondary to that circumstance. Sucking reappears at various ages up to seven years. I wouldn't worry too much up to the age of four or five years. When the child gets to be about six or seven you can begin to take him into your counsel, but not through reading him a lecture or through laying down the law. The wise parent even goes into something of a conspiracy with the child. If there's an understanding between mother and child, the father isn't going to hear about it. The child is permitted, perhaps just at first to have a little thumb sucking just before he goes into sleep and then there are gradual substitutions and through an understanding between mother and child you taper off thumb sucking.

Dr. F. H. Maurer—Peoria, Ill.: What about the problem of bad eating habits? I find that a youngster who has eaten well from one and one-half to two years of age begins to assert his authority and may become a bad eating problem.

Chairman Gesell: Appetite changes and fluctuates from one age to another. In our experience, eating problems are now tending to diminish in number. They used to be standard problems of the nursery school. Certainly each problem has to be considered on its own merits. The child's desire to finger feed and even to mess things up can be gratified by common sense arrangements and that sometimes helps. A great many of the feeding problems are reflections of the adult's attitude and if you circumvent the tension of parents, you can set up a more normal condition. Since appetites for different kinds of food tend to vary with maturity level, and this again bears on the developmental factors, so called problems are transitory. The variations in appetite are not as whimsical as they seem.

Dr. Amatruda: Mothers often need considerable reorientation in their attitude toward feeding their children. The over-conscientious mother tries to feed her child too much, feeling that every added morsel makes for added growth and strength, every morsel uneaten is a token of malnutrition and physical inadequacy. Or it may be the mother's way of imposing her authority on her child; in this case refusal of food is looked upon as stubbornness and a battle of wills ensues.

We try to teach mothers that the healthy, well-adjusted child eats what he needs, with relish and with considerable precision, that the amount may be less than her estimate, and that it may vary from day to day. Mealtimes should be pleasant; songs, stories and games are permissible during the young child's mealtimes if they help make things go smoothly. We sometimes suggest that a mother record what her child actually eats at each meal (and between meals) for a week. Most mothers are surprised and relieved to find that the child is consuming a perfectly adequate diet. Insistence that the child feed himself can create difficulties; we simply advise the mother not to insist, but to be willing to help him as long as he needs help.

If the mother is not trying to force the child to meet standards, quotas and ideals, but is simply trying to have pleasant, relaxed, easy mealtimes, tensions will drop out and feeding problems, so-called, will disappear.

Chairman Gesell: A few feeding behavior problems remain in relation to spoon feeding which are due to poor eye-hand coordination. Perhaps, Dr. Amatruda might refer to cases which complicate cerebral palsy. Minimal types of cerebral palsy often interfere with the larynx, pharynx and swallowing reflex in a very definite way and the baby who shows difficulty in swallowing during the first 16 weeks of life may fall in the category we have been talking about.

Dr. R. L. J. Kennedy—Rochester, Minn.: Have you made any observations on the incidence of eating problems or poor eating habits and what constitutes poor eating habits? Does the problem really reside in the child most of the time, or is it merely in the mind of the parent? If the latter is the case, is it because of the constant exposure of the parent to experts, such as pediatricians and nutritionists, and to the many articles that are published in newspapers and magazines which impress them with the fact that certain amounts of certain foods are essential? Are parents too well-educated along these lines; educated to the point where their own judgment ceases to operate? How often do poor eating habits occur in children of primitive people who have never been exposed to experts?

Chairman Gesell: Your points are well taken because for that matter the mealtimes, number of meals, types of food and length of meals, are certainly determined culturally. Dr. Davis demonstrated in her famous experiment that the children do pretty well if left to themselves.

Dr. Amatruda: If the baby has been brought up on a self-regulating schedule, the mother has learned a good deal about appetite variation. Long before the child is a year old, she knows that there are days when he eats less, that he makes up for it later, and that it all balances with his needs in the long run. This mother isn't going to be as disturbed about a reduction in intake, if and when it comes.

Dr. J. A. Wheeler—Newton, Kan.: Do you recognize a negativistic child and is it an inherited trait or the result of a mechanical disturbance at birth?

Chairman Gesell: Negativism sometimes also called stubbornness and obstinacy, is, like so many things, subject to a great many variations. The two and one-half year old child is supposed to be in a negative phase of development and by the way, at about the age of two and one-half there's a peak in the spanking curve. Why do the spankings come to a peak at that time? It is because at the age of two and one-half years the child is in what might be called the "confused" state of his development. He cannot make a good, firm distinction between yes and no, between come and go, between vanilla and chocolate and between come into the automobile or stay out, between fast and slow, between give and take, push and pull—you see, life is full of two-way alternatives. This child at the age of two and one-half is in a phase of development where every street is a two way street because he's just graduating from babyhood and he's on the way to something else. The result is, that he often seems negative, he is unable to make a clear cut choice between two alternatives, he makes none at all or he makes the wrong choice—opposite or negative choice and he's contradictory in his impulses and in his action. At the age of three years he likes to make simple choices, he is not as negative as he was a half year earlier. He has more power of voluntary choice. He is able to conform and therefore the typical three year child is obedient. He likes to conform. The parents do not realize how difficult these "simple" problems are for the child. They try to solve the problem by making an issue of obedience. A great many problems could be avoided if issues were not made of them.

Dr. Amatruda, Problems of the Handicapped Child:

In the second half of this Round Table Discussion we propose to discuss the problems presented by the handicapped child. Our discussion will include the mentally defective child, the child with motor handicaps as exemplified in particular by the child with cerebral palsy; the child with visual handicaps, and the deaf child.

Obviously the establishing of the diagnosis is the first important factor. All of the handicaps under discussion have very serious implications for the child's future and no parent accepts such a diagnosis easily. A diagnosis is thus in itself not enough; it must be made in such a way that it is convincing to the parents. The parents must feel that the child had a careful, thorough examination by a conscientious and interested physician who has not made up his mind in advance. The examination, to be thorough and complete should include a detailed survey of the child's behavior, as compared with the normal child of comparable age—in other words a diagnostic, developmental examination. Such an examination establishes the maturity of the developing nervous system and it reveals the integrity of the nervous system, exposing injuries and maldevelopments. The develop-

mental examination is a strategic weapon for detecting motor handicaps, sensory handicaps and personality deviations because it is, in essence, a series of functional tests with established normal criteria. And these tests are so administered as to be part of a normal life situation, rather than as something imposed on a struggling, resistant, crying child. They involve simply watching an interested child display his abilities of his own volition. And their abilities are not displayed at haphazard but are elicited in a planned and meaningful way. We offer him a block to pick up, and we watch his head control, eye movements, facial tonicity and expression, the manner in which he mobilizes his interest and attention, how he executes his prehensory approach and grasp, his ability to retain and manipulate the object, to bring his free hand into play, to release. We assess his vocabulary, his response to words and sounds, to persons, strange and familiar. We place an enticing toy at a distance and watch his manner of locomotion, comparing it always with the norms for his age.

In these ways, in conjunction with a detailed history of the gestation period, birth and neonatal period, early development, illness, traumas, unusual experiences, the family situation and history—a diagnosis is arrived at. Supplementary laboratory information is, of course, obtained when indicated, but the child's behavior remains the most tangible and revealing index of the developmental status.

So much for diagnosis; treatment does not need detailed discussion at this point. The treatment of the mental defective ranges from custodial care to vocational training and supervision; the cerebral palsied child needs orthopedic care, the blind and deaf require special educational measures, hearing aids, etc.

The problem, once diagnosis is established, is to so convey it to the parent that treatment is acceptable. The parents must feel that the diagnosis was made with great care. Then they must be told the truth, in as kindly a way as possible but with decision and authority. They must be given an explanation in terms they can understand of the causes and mechanics of the child's handicap, the outlook for the future must be stated in simple language, the rationale and the limitations of treatment should be explained. No loophole of doubt should be left in cases of serious amentia. We have found that if the physician leaves one ray of hope for "recovery," the parents remember that and nothing else.

Casual assurances that the child will "grow out of it" or "snap out of it" are vicious in that they are false and misleading and are always eventually proven to be false, and in that such remarks may build up false hopes and unrealistic attitudes which can assume psychopathic proportions. We have to give the parents the truth about their child and help them to face the truth.

The occasional parent who resists or resents the diagnosis—your child is seriously retarded—or your child is deaf—needs understanding. The physician should not take this reaction as a personal affront to his acumen. The parent is rejecting, not the doctor's wisdom, but the tragedy that confronts him. A diagnosis can never be rammed down an unwilling throat nor is a patient ever helped by an offended doctor. We must understand their reluctance to accept an unhappy diagnosis; we wish we could tell them anything else; we agree willingly to their seeking a second opinion or further tests. It must be realized that it takes time to accept such a blow to one's hopes and dreams, and parents invest their fondest hopes and dreams in their children. A sympathetic offer of time, a chance to see what time will do, and then a re-evaluation of the situation are appreciated by many parents. The parent who accepts a verdict of a serious handicap in his child without agony is rare indeed.

The first reaction that goes with acceptance of such a diagnosis has to do with the parents' own feelings. They are grief stricken—how could it have happened to them, what can they tell their friends? Or feelings of guilt or blame may be evoked. The mother who secretly did not want her baby feels punished as may the father who has committed some indiscretion in the past. The parents who have not been able to love their unresponsive or malformed child feel guilty. Mothers assume the blame for their child's deficiencies pleading inexperience in child training, "Perhaps I didn't teach him the right thing—perhaps I didn't give him enough time." Fathers and grandmothers tend to blame the mother and many mothers suffer deeply from a false onus of responsibility. Or the parents may blame the obstetrician or the nurse or feel that the hospital concealed some misadventure. Guilt and blame feelings should be dispelled. When the full truth is told, all should be absolved.

Because parents are such good people, on the whole, and will go to any lengths to help their

handicapped child, it is not too difficult to steer their thinking and feelings away from themselves and toward the child. It is his handicap, his future that must concern them.

Institutional placement of the mentally defective child, if it is indicated, is urged for the welfare and happiness of the child, to protect him from the excessive demands and thoughtless cruelties of the world, to give him freedom and companionship. Placement should be advised when there are siblings, when the child is active and destructive, and particularly when the parents are very young and just starting out in married life.

With cerebral palsy we find that many parents adjust to the fact of a crippled child by making a grim resolve that their child shall rise above his handicap and achieve great things. The same reaction occurs in the parents of the blind and deaf child. These ambitions, could they be fulfilled, would be a solution for the parent, but they are not necessarily a solution for the child and they are often impossible ambitions. The child must learn to accept and live with his handicap and he can do this only if the parents have done it first and can lead the way. We reduce the child's disability as far as possible, we give him as effective a means of locomotion or of communication as possible, all the education he can assimilate, a vocational training suited to his limitations—all these things. But the driving ambitions of the parents must be modified by the realities of the situation. They must learn to appreciate the enormity of the handicap the child is working against, the extra effort required to achieve so many of the abilities that come so easily to normal individuals. To expect too much is to impose feelings of failure and futility on the already handicapped child. Strenuous programs of training may cause more harm than benefit. The training of the handicapped child takes time, much time and patience, and the parents must be oriented to the long, slow pull.

Simplifying the demands upon the child in the knowledge of his limitations relieves many tensions in the parents and in the child. The irritable, over-active destructive unmanageable ament quiets down remarkably when the demands of the environment are adapted to his abilities. Demands for conformity, obedience, neatness, toilet-control, self-feeding, etc. may be far in excess of the defective child's ability to meet them. He can only respond by going to pieces.

The young, deaf child is peculiarly frustrated by his inability to communicate and understand. He is "disobedient," flares into tantrums and is considered difficult and unmanageable, particularly if his handicap has not been recognized. This sort of problem behavior is almost universal in the young deaf child in a hearing family; but note that it is almost universally absent in the young deaf child if the parents are also deaf. Nor do we see rampant behavior difficulties among the children in schools for the deaf. In both these instances, the environment is attuned to the child's disability. The hearing parents of a young deaf child should communicate with him freely by gesture and pantomime in the early years. The aim is to establish lines of communication to and from the child in the most natural way, as an aid to early socialization and as a basis for all his future learning. The young deaf child can become very out of touch with his environment without this sort of help. And blindness imposes such a barrier between the blind infant and his environment that without extra help and stimulation he is apt to become remote, withdrawn and inactive, his behavior limited and stereotyped. Social contacts are especially important to the blind baby; he should be held a good deal, snuggled, talked to, played with and encouraged to play. He should not be left alone for long intervals simply because he is quiet and uncomplaining and the mother is busy. He should early be included as much as possible in the family circle, and given all kinds of normal experiences. Life should not be too complex or too demanding but neither should it be a vacuum.

The parents' ambition should be that his blind child will become a useful, contented, blind adult; that the deaf child shall become a useful, contented deaf person, rather than a poor imitation of a hearing person. The educational and vocational achievements of both the blind and the deaf are so impressive that much hope can be extended to parents looking into the future for their children.

Most parents of handicapped children feel very lost and alone with their problems, and the physician can render them a great service by maintaining a supervisory interest in their child's progress, even after actual treatment or training has been turned over to other hands. A final step in a mature adjustment in the parents is taken when they can be interested in other handicapped children beside their own. Numerous associations of parents of children with cerebral palsy and other handicaps have been formed in recent years and they have become a driving force moving to secure better therapeutic and educational facilities for handicapped children.

Parents should be encouraged to join such an organization; they meet other parents with the same problems, lose their feeling of isolation and aloneness, gain new perspectives concerning their own child and acquire new insights into the needs of all children.

Chairman Gesell: Just a postscript to this statement—it certainly opens up a very wide field, perhaps one child in 20 is sufficiently handicapped to require special attention. When there is a gravely handicapped child in the family, the pediatrician assumes tremendous importance; because the family turns to him not only for a diagnosis but for guidance. The problem is complex; and often there is no one else to give initial guidance and assistance.

Dr. R. N. Andrews—Mankato, Minn.: The thing that impresses me when the parents of these children come to me is: first, that they have confidence in me, and second they want me to tell them what to do. An attitude of indifference in the doctor is wrong for the parents, the child and for the doctor. You can hold that relationship if you do something for parent and child and if you are considerate and sympathetic; if you take their case as if it were your own child. Let them know that you are interested and you can do a great deal. These patients surprise you with what improvement they make as the months go on.

Dr. Amatruda: You are quite right, of course. Parents cannot simply be dismissed with a diagnosis. The doctor who says bluntly, "There is nothing to do for your child—put him away," only succeeds in antagonizing the parents and in sending them to another doctor, and still another, until they are making the endless rounds of doctors, clinics and chiropractors.

Even if we cannot cure the child, we do not have to be blunt, and if we are sympathetic there is much that we can do for the parents. If they can be made to feel that a careful, thorough examination was made, that your conclusions were arrived at only after all other possibilities were considered, they will accept a diagnosis of serious retardation that includes an explanation, in terms they can understand, of the child's condition. You don't have to leave them false rays of hope for good will's sake; they will stick with you if they feel you have been conscientious, honest with them, and interested in their child, and that you have given them a decisive opinion based on facts. We often have to see these children more than once and work along with the parents until they have made their adjustment. I never feel that my job is done with the family of a defective child until they have solved their problem and seen their solution through. If they have placed the child in an institution, are satisfied with the placement and have picked up the pieces of their family life and started over, a solution has been reached; and for most parents, this is the best solution.

Dr. C. G. Ashley—Portland, Ore.: Do you have any special means of approaching these problems with regard to custodial care? For instance, in our State, we have a waiting time of about a year to get a child into any institution—what should be done for them in the meantime?

Dr. Amatruda: It would be ideal if placement could be made as soon as the parents were emotionally ready for it. In Connecticut the State Schools do not admit children under five years of age; the parents who are well-adjusted and ready to place their child of one or two have years to wait, unless they can afford a private institution. Even so, a good deal is accomplished by making the diagnosis early and by preparing and orienting the parents early. Life is much easier while they are waiting for placement, if the parents understand their child and his limitation; they are not building up false hopes and ambitions, expecting too much of him, creating tensions in themselves and in the child. They are accepting him with sympathetic understanding, and accepting him as he is.

Parents should be encouraged to visit the State Schools and they should initiate and support movements to provide earlier and better care for retarded children. Doctors everywhere should be very conscious of these problems of social welfare and should put their weight behind programs for improvement and expansion.

Dr. Ashley: When we're confronted with the alternative of placing infants in a foster home, a foster mother who may not understand the background of the situation may try to make a good impression by encouraging the parents to feel that the child will be all right. How can she be directed in this matter?

Dr. Amatruda: The same difficulty arises in dealing with some of the private institutions for retarded children. No doubt those in charge are quite sincere and feel they are doing a tremendous amount for the child. They often do succeed in making the difficult child more amenable, quieter, easier to live with, but the basic retardation, which is after all the fundamental problem, remains

unimproved. When the parents, then, receive glowing letters from the school telling of improvement, they should be prepared to interpret these letters correctly.

Thyroid is, of course, always prescribed in cases of outright thyroid deficiency or even when a mild thyroid deficiency is suspected. We do not consider it good practice, however, to give thyroid indiscriminately to any and every retarded child. Thyroid, when administered, should be given as a therapeutic test of thyroid deficiency, with a check on the situation before treatment is begun and a check on the results of treatment; if thyroid proves ineffective it should be discontinued.

The question of using sedatives with difficult, disturbed children comes up frequently. Curiously enough, many of these children are unaffected by the usual sedative drugs; some are quieted by amphetamine sulphate (benzedrine) which is normally a stimulant; in other cases, when the difficult behavior has psychomotor values, one of the anti-convulsant drugs may be effective. One can only make a therapeutic test.

Our experience with prostigmine in cerebral palsy has been, on the whole, disappointing.

A good deal is still unknown on the subject of dominance. Many poorly coordinated children are late in establishing dominance, it is true, but which factor is cause and which effect is often hard to say, nor does it follow that establishing dominance improves coordination.

Dr. Johnson: Consider a child who is eight years old, is an only child, absolutely uncontrollable, has never spoken, makes noises, is very active and, as is usually the case, is extremely strong. He's getting to the age now, where it is almost impossible for his parents to handle him. For several years they have tried to place him in an institution, but because the waiting list is so long, it will be two or three years before they can get him in. Is there any indication for cerebral lobotomy in a case of that kind?

Dr. Amatruda: That is an interesting idea. It has not been tried.

Dr. Wheeler: Should children who are not institutional cases fit into the public school program, starting even with kindergarten?

Dr. Amatruda: The dull child is retarded and can not make normal school progress, but he is not mentally defective and does not require institutional placement, or even special class placement in his early school years. He presents an educational problem that is best solved by delaying school entrance. We advise that such a child enter kindergarten at 6, 6½ or almost 7, spend one or possibly two years in kindergarten and not enter first grade until he is 7 or 8 years old. The parents should be warned that the child's progress will be slow and his marks mediocre, and that some grades may have to be repeated; the teacher is also forewarned so that she is not overzealous about holding the child to the full requirements of the grade. When the child reaches his teens, vocational training should be substituted for academic training.

Dr. Wheeler: What about speech difficulties and defects?

Dr. Amatruda: Corrective speech training should be begun at four and one-half to five years of age, before the child enters school. If the defect is still present at the time of school entrance, the teacher should be asked not to call attention to it, to be considerate about asking the child to recite alone, and to keep teasing and other source of tension at a minimum. Speech training should, of course, be continued.

Dr. Wheeler: When schools of speech corrections are so crowded and the demand is so great that children are on the waiting list a long time, should the parents put them in regular schools and run the chance of an inferiority complex's developing as a result of other children laughing at their attempts at talking?

Dr. Amatruda: Children in kindergarten and in the first and second grades do not pay much attention to speech defects in other children, unless they are very glaring defects. It's when he gets to be eight, nine, and ten years and older that the child with a speech defect really begins to suffer. He should start school at the normal age, and he should be getting treatment and training as soon as possible. The real problem is the lack of training facilities, and the real solution is enlarging the facilities.

Chairman Gesell: There's an interesting point behind the question. People who work with stutterers feel that culture is a very prominent factor. If the culture could relax and take a speech defect, less critically, that itself would be a contribution. Too much is made of early speech defects, just as too much is often made of reading disability in some of these children. The culture keeps pressing too hard and it would help if we took less offense at failure in speech. That isn't the solution, but I think it's part of the story. What are the ages that you were thinking of?

Dr. Wheeler: The age when he would normally enter the public school—about kindergarten or first grade.

Chairman Gesell: The whole trouble with our culture in relation to children is that it isn't flexible enough and we should think much more in terms of service to the children, rather than the maintenance of the curriculum and programs of promotion. If a maladjusted child were permitted to come to school, two or three times a week at the end of the afternoon, or for the listening story period or something of that sort, tension would be relieved for the teacher, for the parents and for the child. It wouldn't be a cure but it would be a partial adjustment and we should begin to use common sense ingenuity in all these problems. Sometimes a great deal can be accomplished with a handicapped child if you get some bright high school girl to come into the picture and give a little help from time to time. Certainly the school should think in terms of individualized service to handicapped children, and the doctors will naturally be behind such a policy.

Dr. H. Medovy—Winnipeg: Would you say more about children with minimal cerebral palsy.

Dr. Amatruda: We see a number of infants whose neuromotor patterns are quite abnormal and yet development is progressing reasonably well. He is going through the usual developmental stages, using abnormal or substitute motor patterns to achieve his performance.

For example, we see a 28 week old infant and place a block in front of him; the normal infant regards it, reaches for it, picks it up and exploits it. This infant looks at it, animates and excites; he wants it but he does not reach for it. If we bring it to his hand, or bring his hand to the block, he grasps it eagerly and manipulates it. He has the whole mechanism for normal exploitation for his age, except the one very important cog, prehensory approach. His hand-to-object mechanism is "out." Another infant of 40 weeks may approach objects well enough but be unable to grasp them effectively. He has the impulse to play with the block and he does play with it, but not by grasping it. He will flick it, tip it, push it about, scratch near it; everything is there but the grasp mechanism. It is interesting too, to note that often grasp is not completely out, but can be elicited in certain contexts. If the block falls off the table he will pick it up, replace it and then begin his tactile exploitation again. Or that same child may be able to pull to his feet by grasping and holding the bars of his crib. Such children need a good deal of help in developing normal play patterns. There are usually other minor motor signs, such as strabismus, a mild facial weakness, or difficulty with swallowing. As these children grow older, motor signs tend to become almost imperceptible. They walk well and use their hands quite adequately; nothing more than a little clumsiness may be noticed. They do, however, seem to have a special tendency to develop personality difficulties.

One interesting boy came to us at the age of five as a difficult boy, with tantrums, nervousness, refusal to feed himself. The mother had had medical advice, "Put the food in front of him. If he won't eat it, let him starve." There had been a continuous battle between this mother and her boy for the past two years, a dreary record of punishments, lost tempers, etc. After the examination I said to the mother, "There are two things about your boy that you didn't tell me." She looked surprised and asked what they were. "The first thing is his hand movements." "Oh," she said, "he's just nervous." Then I asked, "What about his drooling?" "Well, that's because he used to suck his thumb and his teeth are out of line—" and she had explained away, to her own satisfaction at least, two of the boy's most salient symptoms. He had poor control of his oral and pharyngeal musculature, and a very obvious manual incoordination; small wonder that he was having difficulty with eating and with feeding himself!

Chairman Gesell: Did she recall that he didn't swallow when he was a baby?

Dr. Amatruda: Yes. A history of choking on his own saliva until he was about two years old was elicited. We would explain to the parents that this child had sustained an injury to the brain, that the damage to the brain is the cause of the child's difficulties. They should be told that the outlook for walking, talking and general development is good (as in this particular case it was), but that the child is going to need sympathetic understanding.

Dr. Medovy: Do you think that if you stress the cerebral injury to the average parents that probably they will watch every move and step and the child is going to suffer from too much attention?

Dr. Amatruda: I don't want the parents over-concerned, but I do want them to be concerned, and I would consider it a normal reaction. The concerned parent who has some understanding of his child's handicaps is less likely to misinterpret the child's behavior as a disciplinary problem.

Dr. Barrett—Chicago: Would you say something about the normal child who is a stutterer about nine or ten years of age?

Dr. Amatruda: The stuttering seen during the pre-school years is usually on a tensional basis and is apt to be fairly benign. It is quite common. The child of three or three and one-half whose ability to express himself lags behind the volume and urgency of what he has to say, ties himself up into verbal knots. If we can quiet things down for this child, smooth out his whole day, and if the mother can be unconcerned about his speech, the stuttering will drop out promptly. Some of the children who continue stuttering up into the school years could have responded in the same way but were treated by too frontal an attack, with too much attention focussed on the speech defect. The pattern was driven in, set and established by too much treatment, too early. In a certain number of persistent stutterers, I feel sure the speech defect is associated with cerebral injury.

Chairman Gesell: The age of 42 months is worth remembering as one in which this transitional kind of instability occurs. It shows itself in the speech mechanisms and in other ways. In the use of a crayon there are more wavering lines, more tremulousness. This goes to show that this is a period of partial disequilibrium in the development of the action system. That's why it is well to recognize it as a transitional phase and not bear down too heavily upon what looks like a speech defect but may well never become so if the apparent defect does not receive unwise attention.

Dr. Maurer: When a child 18 months of age, just beginning to walk, makes no attempt to grasp any object put in front of him, is it due to neglect in handling or would you rather suspect a minimum cerebral damage?

Dr. Amatruda: I would like to see the child, and I would like to know more about his personal history. You may be dealing with two factors; the symptoms of minimal injury are tremendously distorted and exaggerated under institutional condition of impoverished environment. I would suspect that you are dealing with some such situation.

Dr. J. C. Jaudon—St. Louis: Do you not occasionally see a child who is very slow in development, but who turns out to be perfectly normal?

Dr. Amatruda: One often does suspect environmental factors in a case such as you have described, even if there is nothing that you can put your finger on. They are not common, but we do see them.

We usually make a diagnosis of minimal injury in infancy or early childhood, follow their development and know their potentialities, weaknesses and limitations well before they are ready for school.

Chairman Gesell: We are obliged to bring this discussion, which has been stimulating to us to a close. I think that we agree the physician should lend his moral support to the setting up more flexible services for all handicapped children particularly those of pre-school age.

Pediatrics

VOLUME 1 APRIL 1948 NUMBER 4

SPECIAL FEATURE SECTIONS

THE PEDIATRICIAN AND THE PUBLIC

EDWARDS A. PARK, *Editor*

For sometime I have been anxious to obtain for the Column the views of members of the Academy who hold what might be termed the extreme conservative opinion on questions pertaining to medical care. Now this has happened for Dr. Black allows his circular letter sent informally to each member of the Academy to be printed (below) in the Column. All readers of Dr. Black's letter will agree that as a challenger in the lists he has struck with naked lance point and loud clang the shield of the Committee for the Improvement of Child Health,* who are the authors of the report, and at the next moment the shield of the Executive Board which approved it. Dr. Black's letter deserves the fullest prominence for the reason that it expresses the opinions and also the very strong feelings of a member of the Academy and in addition because its viewpoints are so diametrically opposed to those of the Academy Committee and of the Executive Board.

In the letter which follows Dr. Black takes three main positions. The first is by implication rather than direct statement that, since pediatric training and child care in this country rank "the best in the world today," they are satisfactory and do not require change. I think that this debatable subject need not be discussed in the Column, for the only real question at issue is whether pediatric training and child care are as widespread and good as they can be made to be in the United States. It is regrettable that the full report of the investigations of pediatric education conducted by the Committee could not have been published coincidentally with the Committee's recommendations and Dr. Black have had the benefit of them before he wrote his letter. The Committee has gathered together after great labor a mass of facts such as have never existed previously and possesses a knowledge of the subject which is unique in this country. It is obviously premature and hence foolish to attempt to come to any conclusion concerning the adequacy or inadequacy of child health services, including pediatric education, until the Committee's facts are presented. It is entirely possible, is it not, that the data may be so overwhelming as to make the question futile. A second position which Dr. Black takes is that the authors of the recommendations are not adequate as Academy representatives and he goes so far as to recommend that another committee should be appointed which would approach the problem "realistically." This, of course, is a matter which must be left to the Academy members and nothing is to be gained by a discussion of it in the Column. The third important stand which Dr. Black takes is that the principle of acceptance of federal money for the improvement of pediatric education is so dangerous as to be unjustifiable quite irrespective of any need, for the reason that it is a step toward socialized medicine. This is the fundamental issue raised by Dr. Black and the one which should be discussed in this Column.

When I talk with my friends who are the heads of medical schools or of privately endowed hospitals, I find them alarmed over the future. They see no other way of meeting expenses under present economic conditions except either to obtain state, federal or federal-via-state support to offset the loss of voluntary contributions on which they have so depended for their sources of revenue in the past, or else to make the schools and the hospitals self-supporting. If the hospitals are reorganized so as to be self-supporting, the cost of complete medical care becomes so great as

* See page 522 for further ICH information.

to be out of the reach of all except the well-to-do. If the medical schools are obliged to become self-supporting, it is inevitable that the cost of medical education to the medical student will be greatly increased and also that the standards of medical education will be lamentably lowered. The issue obviously extends far deeper than Dr. Black's challenge indicates and cannot be answered by any hasty superficial consideration. Times have changed. It is impossible to recreate the past though the temptation to try is very great and it is, therefore, necessary to make some kind of adaptation to the present.

E. A. P.

March 19, 1948*

Dear Fellow Member of the American Academy of Pediatrics, Fellow American Physician, and Fellow Citizen of America:

If you have in your heart any love for *personal freedom;* if you have any love for *free American institutions;* if you believe in the *integrity and dignity of the individual;* if you believe that the children under your care (and your own children) have a right to grow up as *free individuals* and to take their place eventually as citizens of a great free society where they may seek their own destiny, not hampering others and unhampered by others, then *please* take time to read *carefully* this critically important letter which I am able to send to you through the instrumentality of the Association of American Physicians and Surgeons.

You have recently received, under date of March 2, 1948, a form letter from our President, Dr. John A. Toomey, with an attached seven page report of our "Committee for the Improvement of Child Health." My purpose in this present letter is to strip this report of it fatuous platitudinous nonsense; expose its basic collectivist philosophy, analyze its recommendations and show how, if adopted by the Academy, they will lead inevitably to federal domination of medical education and training and advance us all a long, long way toward Federal domination of Medicine, i.e., Socialized Medicine. It is my fervent hope that this letter, plus your own personal study of the report, will lead you to a full recognition of the disastrous implications which it contains and a strong personal determination to see that it is promptly relegated to the waste basket where it most certainly belongs.

I. The Essence of the Report

Stripped of its beguiling platitudinous nonsense the report may be reduced to the following essentials

1. It is a recommendation by an official committee of the American Academy of Pediatrics for FEDERAL (i.e. TAX) support for pediatric education, *which has been already* approved by the Executive Board of the Academy of Pediatrics in Chicago on February 8, 1948.
2. The report states that

---

* Note received April 9, 1948: On request of several Fellows of the Academy of Pediatrics the following general letter which I sent recently to all members is being published for the benefit of those who may not have received or read the original. I wish to have it clearly understood that my reason for indulging in such inflammatory, strong, provocative, and unrestrained language in this general letter and in my letter to Dr. Toomey is to stir the rank and file of Fellows from their natural lethargy, to excite them to thought, expression of opinion and to action. The desired result has been achieved. I am personally convinced the subject is of prime importance not only to every one of us, but also and to an even greater degree to those who shall follow us.

I should like to have an opportunity soon to prepare a more detailed statement couched in more restrained and appropriate language, to provide the membership with a better understanding of the implications of federal subsidization of pediatric education.

If the executive board of the Academy fails to rescind its approval of the report in question before May 1, 1948, the National Health Conference in Washington, D.C. will make the most of our ill-advised approval. Headline: "BY THEIR OWN FIGURES DOCTORS PROVE INADEQUACY OF CHILD HEALTH CARE. ACADEMY OF PEDIATRICS URGES EMERGENCY FEDERAL LEGISLATION."

(signed) Wm. C. Black, M.D.

(a) There are not enough well-trained doctors in America to care for our child population.
(b) The vast majority of doctors now caring for American children are grossly incompetent because of the inadequate training.
(c) The doctors are poorly distributed.
(d) Medical Schools and Hospitals do not have enough money to educate pediatricians.
(e) The cost of adequate pediatric education is prohibitive. Even the Murray-Wagner-Dingell Bill if passed wouldn't bring Utopia in child health because there are not enough good pediatric trained doctors properly distributed to service it.

Therefore, this vicious, dangerous unAmerican report concludes:

(a) Federal (i.e. tax) money for medical school pediatric training is a most urgent and immediate need.
(b) Federal (i.e. tax) money is immediately necessary or some pediatric training hospitals will have to close their doors, others will remain ineffectual.
(c) Federal (i.e. tax) money must be used as a bribe for pediatric students to get them to be forced to settle in rural areas after they are trained.

This may be summarized as follows: The Executive Board of the Academy has approved a Committee report based on our national survey which states that Utopian care for all American infants and children can certainly be provided if the Federal Government will pay for educating and training enough doctors and then forcing them, by devious and dishonorable means, to practice in the localities where such services are deemed needed; whereas at present the physicians caring for children in America are, on the whole, grossly incompetent because of inadequate training and are so poorly distributed that vast numbers of American children are denied "those very services which have been agreed upon as the RIGHT of every child: the essential preventive, diagnostic, and curative medical services of high quality." Finally, "neither grants-in-aid to states for medical services nor *compulsory health insurance* will effect better or more evenly distributed medical care until well-trained physicians are available to render that care, especially in areas of need."

II. Analysis of the Recommendations

The bald, brazen, unqualified recommendations in this report are that Federal Tax Money be appropriated *under the* FEDERAL SECURITY ADMINISTRATION to subsidize medical schools, other educational institutions, and students. The FEDERAL SECURITY ADMINISTRATION should appoint an advisory council of nine members who would have absolute control.

III. The Basic Collectivist Philosophy of the Report

There can not be one shred of doubt in any reasonable person's mind that the basic philosophy of this report is clearly, unequivocally, baldly, completely, and uniformly COLLECTIVIST. If it were adopted by the Academy and the legislation to render it effective were enacted by Congress, control of pediatric education in the United States would pass into the hands of the Federal Security Administration *which is world headquarters for Socialized Medicine!*[1-4] Those who would regiment the medical profession and the people[1] would not have forced their foot in the door—we would have opened it widely for them! I grant you control would not be complete at first, but it would come as irresistibly as an avalanche in a few years.

Please note the following pertinent and commanding facts:

(1) There is *not one word* in this report concerning the paramount fact that the American child is the healthiest best cared for child in the world today or in any other large country in the history of the world.[5]
(2) There is *not one word* in this report to indicate the amazing progress of American medicine generally and pediatrics specifically during the last century.[5]
(3) There is *not one word* in this report to mention the certain fact that pediatric training in the United States today is by far the best in the world, the best the world has ever seen.
(4) There is *not one word* in this report to point out that the very real difficulties of our educational institutions generally and our medical educational institutions specifically are the direct result of three things and three things only:
   A. TAXES TAXES TAXES[2]
   B. The ghastly expense, waste, and disruption of World War II.
   C. The veterans' education program.

Conclusions

I can draw no other conclusion from this report than that the results of our survey, with which nearly every one of us cooperated wholeheartedly and honestly, are immediately being perverted, distorted, twisted, and prostituted to the frank, bold, shameless, support of an idealogy as foreign to everything which has gone to make American medicine what it is today—to make America what she is today—as were the tactics and philosophy of Hitler and Mussolini.[2,3,5,6,7] This report, which would picture the medical care of American children as grossly inadequate, can only be drawn by comparing our present *real* status with an ideal, unreal, Utopian, starry-eyed-dreamer's view of a never-yet-attained state of perfection.[5] The *real fact* of the excellence of life for America's children and the enormous expansion of America's child care compared with that of any other country is completely ignored! The authors of this report must be either stupid, or visionary, and our Executive Board, which approved the report, must suffer from one or both of the same disastrous defects. It is up to us, the common members of the American Academy of Pediatrics, to make ourselves heard in the high places of our organization *immediately* and with such vigor and unanimity that this report *in its entirety* will be disapproved and heartily condemned, and another committee appointed which will approach this problem realistically.

The approval of this damnable report by the Executive Board of the American Academy of Pediatrics places us squarely in the disgraceful, unenviable, and intolerable position of being the first organized group of reputable and honorable American physicians to endorse officially a report and recommendations which are as unAmerican as the machinations of the Kremlin. This insult to ourselves, to our fellow American Physicians, to this great free nation of ours—this desecration of LIBERTY must be promptly, decisively, and completely wiped from our record or I, for one, shall resign from the Organization. Fellow member of the once American Academy of Pediatrics, we have been most disgracefully betrayed!

For all of you who see the full and hideously dangerous implications of this report I suggest the following procedures:

(1) Write your opinion immediately to your District Chairman, to our President, or both, demanding an immediate emergency meeting of our Executive Board to rescind its approval of the report and then pass a strong resolution of total condemnation.

(2) Send a copy of your letter to me and the Association of American Physicians and Surgeons will give nation wide publicity to the tabulated results.

(3) Inform your colleagues (members and non-members of the Academy) of the nature of this report, discuss it, and publicize as widely as you can its total condemnation.

For those of you who may not sense the full importance of the report I append a bibliography for your further study and enlightenment. Obtain and read this material promptly, then send in your letters as soon as possible. You may receive promptly the entire bibliography (except books 7 and 8) from the Association of American Physicians and Surgeons, 360 N. Michigan Avenue, Chicago, Illinois, at a cost of $1.35.

For those of you who will not think or act I can do nothing except to hope your numbers are few and that your awakening will not be long delayed.

Fraternally yours,

Wm. C. Black, M.D.
Fellow, American Academy of Pediatrics
President, Association of American
Physicians and Surgeons.

P.S. Some of you who are not yet members of A.A.P.S. may wonder why the Association of American Physicians and Surgeons, the national "grass-roots" association providing democratic representation for the medical profession in medical economics, public relations, and medical legislation *as they affect the public good,* is willing to sponsor this communication. All I can say in answer is that A.A.P.S. is the *only* agency of, for, and by the physicians of America that can and does take positive, prompt, and effective action in matters of this sort. I am enclosing for your information the A.A.P.S. "Thirty Questions and Thirty Answers."

P.P.S. I am also enclosing a copy of my personal resignation from the American Academy of Pediatrics to be effective when and if the Academy approves this report or any part thereof.

W.C.B.

BIBLIOGRAPHY

1. Shearon, M.: "Blueprint for the Nationalization of Medicine—Plans to Enchain Medicine by Unwarranted Regulative Interference." Shearon Medical Legislative Service, 610 Columbian Building, Washington 1, D.C. Single copy 25¢.
2. Harper, F. A.: "Thirty-one Cents." Foundation for Economic Education Inc., Irvington-on-Hudson, New York. Single copy—no charge.
3. Hunt, B. K.: "Show Me Any Other Country—." Foundation for Economic Education, Inc. Irvington-on-Hudson, New York. Single copy—no charge.
4. Harness, Forest A. (Congressman): "Publicity and Propaganda in the Government Agencies and Bureaus." Bulletin of the Assn. Am. Phys. & Surgeons, Vol. 5, No. 1, Pages 5-14. Feb., 1948.
5. Shearon, M.: "Paradise Unlimited! The Menace of the Police State." Shearon Medical Legislative Service, 610 Columbian Building, Washington 1, D.C. Single copy 25¢.
6. Von Mises, Ludwig: "Planned Chaos." Foundation for Economic Education, Inc., Irvington-on-Hudson, New York. pp. 90, 1947. Single copy 65¢.
7. Hayek, Friedrich A.: "The Road to Serfdom." University of Chicago Press, Chicago, Illinois, 1944. $2.75.
8. Stern, Bernard J.: "American Medical Practice in the Perspectives of a Century." The Commonwealth Fund, New York, 1945. $1.50.

TRENDS

IN HEALTH LEGISLATION AND ADMINISTRATION

This and subsequent descriptions of events and trends are intended to be unbiased and factual, presenting both sides of controversial matters so that conclusions may be formed from critical appraisal of things as they are. These statements do not necessarily reflect the opinion of the writer, nor are they to be interpreted as official opinion of the Academy.

THE pace has been a fast one during February in federal planning for the nation's health. So much has happened that only a few of the significant developments can be reviewed briefly:

National Health Assembly

In January, President Truman addressed a letter to Mr. Oscar Ewing, Federal Security Administrator, calling for a ten-year health plan. Following closely upon the receipt of this letter Mr. Ewing announced at a press conference on February 13th, that a "National Health Assembly" will be held in Washington, May 1st to 4th, "to see what we have; to know accurately the health facilities and personnel of the nation and of each community; to determine what we need—the difference between the two showing us our health deficits; to devise feasible methods of meeting these deficits." The immediate benefits to come out of the Assembly were described as "a guide to community action for local health improvements; a detailed practical pattern of cooperation among all organizations operating in the health field—public and private, national, state and local; and a more detailed and specific knowledge of our present health picture and of the job that has to be done to improve it." (Note: It seems timely to point out that the Academy, first through its Study, and now through its Committee for Improvement of Child Health, is already out in front with respect to very similar objectives.)

Federal Aid to Medical Schools

On February 17th, Mr. Ewing first made public the intention of the FSA to develop a federal aid program for medical education. Nine days earlier the Executive Board of the Academy unanimously voiced its own approval of an Academy proposal for federal aid for pediatric education with unrestricted grants made directly to medical schools to be used as directed by the head of the department of pediatrics for the purpose of giving more adequate training to physicians in the medical care and health supervision of children. (See Report of the Committee for Improvement of Child Health).

Addressing the National Health Council, Mr. Ewing stated: "I am convinced Federal aid to medical schools and to medical students is essential if we are to have the doctors necessary for the health and well-being of our people." He presented an outline of what Federal legislators should provide as follows:

"First, a Congressional finding that we suffer from a shortage of doctors, dentists, nurses, and other health personnel essential to maintaining the nation's health, and that this shortage is aggravated by the inability of many qualified individuals, particularly members of minority groups, to obtain professional training.

"Second, a declaration of national policy to increase the number of doctors, dentists,

nurses, and others to serve the American people, and to take such steps and use such Federal resources as are necessary to overcome shortages in these fields. I believe the only justification for a program of special aid for medical schools at this time is assurance that it will help to meet the serious doctor-deficiency facing our Nation.

"Third, a clear-cut and unambiguous declaration that opportunities made available under the bill be open for all qualified individuals, without discrimination because of race, creed, color, or national origin.

"How do we propose to accomplish these aims? By three types of programs:

"*First, grants for operating expenses.* We contemplate a program of grants of approximately $50,000,000 annually to schools of medicine, dentistry, nursing, and public health. This is considerably less than the medical school deans say is necessary, but I believe it will be a good start. These grants would be available for hiring staff, operating facilities, and buying equipment.

"As an example of how these funds might be distributed, the bill might assure each 4-year school of say a flat $100,000 each year. In addition, each school might receive a further amount based upon the number of students, thus creating an incentive for increased enrollments.

To be eligible for such grants, a school must give assurance—

that it is training the maximum number of students, of which its facilities and resources are capable, consistent with acceptable standards;
that it will not impose unreasonable restrictions on non-residents awarded scholarships under the program; and
that it admits students without discrimination on the basis of race, creed, color, or national origin—except that where segregation of Negroes is required by law, a showing must be made that comparable educational opportunities are provided for Negroes.

"No grant would exceed 50% of the cost of instruction in the school during the year.

"*Second, grants for construction of medical schools.* Since it has not been possible in advance to estimate the amounts of money that would be needed, the size of this part of the program might well be left, at this stage, to annual determinations through appropriation requests.

"Applications for the grants would have to give assurances identical to those I have already outlined, and grants would be made in the order of their effect in alleviating the shortage of medical and health personnel. These grants, too, would not exceed 50% of the total cost.

"*Third, scholarships.* I have in mind two types of scholarship—a State scholarship for doctors, nurses, dentists, and public health personnel who could practice anywhere they wanted; and a National medical scholarship for doctors who agree to serve for a time in special shortage areas.

"The State scholarships would be made possible through grants to each of the States, for a total of 10% of the doctors, dentists, nurses, and public health personnel enrolled in such professional schools. This would assure all parts of the country the opportunity for improving the health service available to their residents. No State should receive this grant unless scholarship selection is made without discrimination for reasons of race, creed, color, or national origin. The amount of a State scholarship would include tuition, books and fees, but not room and board.

"The National medical scholarships would not exceed 600 annually, and would

be available to doctors who agreed to serve for some period in Federal medical establishments—such as the Veterans Administration, the Public Health Service, the Army, and the Navy—or in State and local health agencies—as, for example, in doctor-shortage areas designated by State health authorities. Selections would be made by a top-flight Medical Scholarship Board composed of representatives of the medical and education groups, and the public. These scholarships would cover tuition and would also include $90 a month for living expenses.

"Needless to say, the bill should clearly provide that no Federal employee may exercise control over the professional standards, academic qualifications, curriculum, or administration of any medical school."

Local Public Health Services Act

A bill (S-2189) has been introduced by Senator Saltonstall to assist States in "developing and maintaining local public health units organized to provide basic full-time public health services in all areas of the Nation and in the training of all types of personnel for local public-health-unit work." In introducing the bill Senator Saltonstall stated:

"The purpose of the bill is to have the Federal Government assist States and localities in providing better public health services. At present less than 10,000,000 of our total population live in areas served by local units which meet basic requirements of public health standards, while more than 40,000,000 persons in the United States live in areas not served by any local public health units. I believe this fact alone calls for careful consideration by Congress.

"I wish to make it perfectly clear that I am opposed to the socialization of medicine. I am not in favor of interfering with the freedom of action of individual doctors."

The Children's Bureau Reports

In an annual report* the Children's Bureau reviews services rendered during 1946-47, additional needs to be met and expansion planned.

Under the heading of "Improving Services for Mothers and Children" the report describes the job yet to be done for the children of the nation:

"The great gaps now existing in the maternal and child welfare services will disappear only when there is full public acceptance of responsibility for seeing that facilities are made possible for continuous study and investigation of the causes and the extent of need, and that services known to be necessary to protect and maintain the health and well-being of mothers and children are within reach of all mothers during maternity and of all children wherever they may be living. . . .

"To close them (the gaps), legislation must be ample in scope and must provide for adequate financing of services. It must provide for progressive development of the full range of health and welfare services for parents and children; for care of high quality; for training of personnel in the special fields of service; and for parent education in the essentials of good care. Such services should be provided without discrimination as to race, creed, nationality, residence, citizenship, or economic status."

* Annual Report of the Federal Security Agency, Section One, Social Security Administration, 1947, U. S. Government Printing Office, Washington, D.C.

PUBLIC HEALTH, NURSING AND MEDICAL SOCIAL WORK

LEONA BAUMGARTNER, *Contributing Editor*

PRINCIPLES FOR CONSIDERATION IN JUDGING THE PROBABLE EFFECTIVENESS OF FEDERAL LEGISLATION DESIGNED TO IMPROVE THE HEALTH OF CHILDREN OF SCHOOL AGE

Principles Relating to Scope and Content

1. The only criterion against which legislation can be measured is that it promotes continuing improvement in the health status of school-age children. Many factors are involved. Specific legislation, however, is likely to be concerned with only certain phases. Three of these needing legislative attention at this time are:*
   1) Health instruction and physical education
      Here are included those organized programs within the school providing learning experiences in personal and community health, and instructional and practice periods of physical activity.
   2) Health examination services
      Here are grouped those activities of physicians, dentists, nurses, teachers, and other professional personnel through which the health status of school children is appraised and diagnostic service begun.
   3) Treatment services
      Here are grouped the activities of physicians, dentists, nurses, and other health personnel; health department or other public agency; preventive, diagnostic, and treatment facilities; hospitals, clinics, and other community agencies which provide preventive, diagnostic, and treatment services to children.
2. These three phases are so closely interlocked that planning and provision for all of them are necessary in order to make maximum contribution to the health status of children. Legislation concerning any one or all of these should be evaluated in terms of principles contained in this statement.
3. These activities can be best carried out when the community provides:
   1) adequate school facilities with sufficient trained professional personnel to meet the educational needs of all children in the community.
   2) a community health program which includes an organized local health unit

---

Proposed by the Committee on Legislation, School Health Section, A.P.H.A., December 8, 1947. Approved by School Health Section Council, January 9, 1948.

(See Special Report from the Committee on School Health to the Executive Board in this issue's Academy Proceedings and Reports Division for comment.)

* It is recognized that rehabilitation and vocational training of the physically handicapped is an essential in providing for the total health needs of school children. Appropriate rehabilitation representatives should be consulted in making plans. Moreover, existing legislative and administrative provisions established on both federal and state levels under Public Law 113 to carry out these services should be utilized and such amendments and additional appropriations as are necessary should be made to enable Federal and State Bureaus of Vocational Rehabilitation to provide services to all who come under their jurisdiction.

adequately staffed with full-time personnel and physicians, dentists, nurses, and other health personnel available in the community.

3) facilities (hospital, health department, and other preventive, diagnostic, and treatment facilities) for necessary preventive diagnostic and treatment services accessible to children from infancy through childhood.

Principles Relating to Health Instruction, Physical Education, and Health Examination Services

4. The general policies, organization, and plans for execution of the program should be planned jointly by the appropriate educational and health authorities at the federal, state, and local levels, after consulting with professional and other groups concerned.
5. Legislation should be sufficiently flexible to enable it to operate in accordance with a variation in state laws and administrative patterns.
6. Coordination at the federal level should be brought about through a joint committee representing the U. S. Office of Education, the U. S. Public Health Service, and the Children's Bureau, which shall give joint consideration to and advise the Federal Security Administratior on the establishment of policies and regulations, the basis for approval of state plans and recommendations regarding the allocation of funds. State superintendents of education and state health officers shall be consulted before the establishment of federal policies.
7. Legislation should contain provisions concerning purpose and scope of the program, general organization, and administrative structure. Details regarding operation and content of the program are matters for state planning in harmony with the general purpose of the legislation.
8. Education is the function of the schools. Safeguarding and promoting the health of the community is the function of health departments. The education departments should have full responsibility for the instructional progress, administrative responsibility for the conduct of all activities taking place in the schools, without regard to which agency operates the program of health examination services. Where health examination services are operated by education departments the health department should be responsible for the professional consultation needed for establishing and maintaining standards, stimulating continued professional growth, and integrating the health service program in the school with the health program in the community.
9. All personnel rendering health services must be properly supervised by qualified members of their own profession.
10. The provision for consultant services on federal, state and local levels should be planned jointly by educational, health, and rehabilitation authorities so as to avoid overlapping and duplication of services, and so as to gain participation and cooperation by all who serve children.
11. Funds should be allotted to the states on the basis of a single plan submitted jointly by state departments of education and of health after consulting with educational, medical, dental, nursing, and other professional groups concerned within the state.
12. Funds must be used for the initiation of new programs and services and the

extension and improvement of existing programs. They must not be used to take the place of present expenditures from state and local sources.

13. Funds made available must be expended through public agencies under public control.
14. The same quality of health instructional programs, and health examination and diagnostic service for school children should be available to children without regard to race, color, creed, nationality or economic status.
15. Funds should be distributed so as to serve all children of school age insofar as the amount of funds allotted permit and with appropriate safeguards for the quality of service rendered.

Principles Relating to Medical Treatment Services

16. Plans for the extension of medical treatment services for school-age children should be developed by state health authorities in cooperation with medical, dental, nursing, educational and other professional and lay groups concerned in each state.
17. Federal funds are necessary to assist the states and local communities to provide medical treatment services for children of school age. Existing legislative and administrative provisions established on both federal and state levels to carry out appropriate sections of the Social Security Act should be utilized and such amendments and additional appropriations as necessary should be made to enable the Federal Security Agency and the states to assist in development of necessary medical treatment for children of school age.

NEW COMMITTEE ON CHILD HEALTH FORMED IN THE AMERICAN PUBLIC HEALTH ASSOCIATION

The American Public Health Association has just announced the formation of a Committee on Child Health with which, it is planned, the American Academy of Pediatrics will have close working relationships. The plan for such a committee was formulated after consultation with various members of the Academy, particularly members to Dr. James L. Wilson's Committee for Improvement of Child Health. It was felt that there was great need to have health officers and other members of the public health professions become more interested in matters related to child health. The Academy Study will obviously produce a great deal of material of interest to the public health profession. Moreover, the Academy may well turn to the American Public Health Association for guidance concerning and implementation of certain recommendations that may come out of its report.

The plan indicates the following purpose of the new Committee:

"To consider matters related to the health and medical care of children and to maternity care and to act for the American Public Health Association in its relations with national organizations and agencies, professional or nonprofessional, that are concerned with the advancement of child health, having due regard for the work of the Sections and of other committees of the Association. This would include the development of recommended standards, procedures and policies and development of relationships with such organizations as the American Academy of Pediatrics, the Federation of Obstetrical Associations, the American Medical Association, the National Education Association, the American School Health Association, and the National Congress of Parents and Teachers."

The following committee has been appointed: Leona Baumgartner, M.D., Chairman,

Director, Bureau of Child Hygiene, New York City Department of Health; Margaret Adams, R.N., Instructor in Nursing Education, Teachers College, Columbia University; Allan M. Butler, M.D., Massachusetts General Hospital, Boston; Richard F. Boyd, M.D., Director, Local Health Administration, Illinois State Health Department; Edwin F. Daily, M.D., Director, Division of Health Services, U.S. Children's Bureau; Mayhew Derryberry, Ph.D., Chief, Health Education and Training, U.S. Public Health Service; Paul Harper, M.D., Associate Professor, Department of Public Health Administration, Johns Hopkins School of Hygiene and Public Health; Herbert R. Kobes, M.D., Director, Division of Services for Crippled Children, University of Illinois; Frank Stafford, M.S., Specialist for Health Instruction, Physical Education and Athletics, U.S. Office of Education; Frederick J. Stare, M.D., Associate Professor, Head of Department of Nutrition, Harvard School of Public Health; Myron Wegman, M.D., Professor and Director, Department of Pediatrics, Louisiana State University School of Medicine; J. M. Wisan, D.D.S., American Dental Association; Kent A. Zimmerman, M.D., Consultant in Mental Health, California State Department of Public Health.

INCIDENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES FEBRUARY 1-28, 1948

The accompanying table summarizes the incidence of nine important communicable diseases, based on weekly telegraphic reports from State health departments. The reports from each State for each week are published in *Public Health Reports* under the section "Incidence of Disease."

Diseases Above Median Incidence

Influenza: For the four weeks ended February 28 there were 45,556 cases of influenza reported. Of the total cases, Texas reported 17,201, South Carolina 4,336, California 4,273, Arizona 3,696, Virginia 3,577, Arkansas 2,079, Alabama 2,050, Oregon 1,870, and Washington 1,345 cases—a total of 40,427 cases, which was about 89% of the total cases. The high incidence of this disease has been confined to the South Atlantic, South Central, and Far Western sections. In the Pacific section the number of cases was 13.8 times the median; in the South Central and Mountain sections the numbers of cases were more than twice the median and in the South Atlantic section the incidence was 1.3 times the median. Few cases have been reported from the North Atlantic and North Central regions. While the number of reported cases declined only slightly from the preceding four weeks, during the last week of the current four-week period, the incidence fell in practically all of the above mentioned States.

Measles: There were 58,759 cases of measles reported for the current four weeks as compared with 20,417 in 1947 and a median of 48,914 cases for the corresponding four weeks in the five preceding years. Most of the current increase was due to an excess of cases in the East North Central and West South Central sections; in the former section the current incidence was more than 3 times the median while in the latter section the number of cases was 2.4 times the median. In each of the other seven sections the number of cases was about equal to or lower than the seasonal expectancy.

Diseases Below Median Incidence

Diphtheria: For the four weeks ended February 28 there were 834 cases of diphtheria as compared with a 5-year (1943-47) median of 1,165 cases. The median was represented by the 1947 incidence. In the Mountain section the number of cases (105) was 62% above the median and a negligible increase was reported from the South Atlantic section, but in all other sections the incidence was relatively low. Of the total cases reported from the Mountain section 31 occurred in Arizona and 23 in Colorado.

Meningococcus meningitis: The incidence of this disease during the current four weeks was slightly higher than that in 1947, but the number of cases (354) was only about 34% of the 1943-47 median

NUMBER OF REPORTED CASES OF 9 COMMUNICABLE DISEASES IN THE UNITED STATES DURING THE 4-WEEK PERIOD FEBRUARY 1-28, 1948, THE NUMBER FOR THE CORRESPONDING PERIOD IN 1947, AND THE MEDIAN NUMBER OF CASES REPORTED FOR THE CORRESPONDING PERIOD, 1943-47

Division	Current period	1947	5-year median	Current period	1947	5-year median	Current period	1947	5-year median
	Diphtheria			Influenza*			Measles		
United States	834	1,165	1,165	45,556	15,707	18,939	58,759	20,417	48,914
New England	27	75	30	17	65	127	2,290	6,036	5,527
Middle Atlantic	82	166	116	48	63	118	12,058	3,444	13,341
East North Central	130	176	160	472	169	477	22,596	3,471	7,455
West North Central	47	97	97	436	228	235	5,310	438	4,196
South Atlantic	166	160	163	8,918	3,893	6,738	3,294	3,376	3,298
East South Central	78	114	106	2,887	503	1,372	1,291	301	2,494
West South Central	129	169	232	20,503	8,484	9,817	6,492	786	2,669
Mountain	105	59	65	4,787	2,147	2,147	1,567	1,661	1,934
Pacific	70	149	156	7,488	155	542	3,861	904	3,874
	Meningococcus meningitis			Poliomyelitis			Scarlet fever		
United States	354	322	1,034	111	185	143	9,626	11,017	16,265
New England	23	13	41	2	7	3	702	1,038	2,036
Middle Atlantic	66	83	213	18	19	15	2,433	2,835	3,798
East North Central	45	42	151	9	30	9	3,258	3,391	4,181
West North Central	29	27	70	9	19	12	855	1,027	1,602
South Atlantic	44	44	161	29	26	21	676	742	1,159
East South Central	48	23	107	10	13	13	375	447	590
West South Central	41	43	94	8	17	15	217	236	506
Mountain	7	7	22	11	4	7	374	440	1,008
Pacific	51	40	107	15	50	34	736	861	1,100
	Smallpox			Typhoid and paratyphoid fever			Whooping cough		
United States	14	13	43	149	167	208	8,556	10,259	9,357
New England	0	0	0	9	10	10	711	1,147	1,141
Middle Atlantic	0	0	0	22	23	33	1,235	2,072	1,925
East North Central	4	5	16	31	23	23	1,725	2,597	1,625
West North Central	2	2	4	4	8	8	500	372	385
South Atlantic	1	0	2	34	31	38	1,035	1,219	1,246
East South Central	1	4	4	5	15	21	369	381	381
West South Central	5	1	15	23	29	38	1,643	1,545	1,181
Mountain	1	0	3	7	11	11	789	318	430
Pacific	0	1	1	14	17	17	549	608	608

* North Carolina, New York, and Pennsylvania excluded; New York City and Philadelphia included.
Data furnished by the Division of Public Health Methods, United States Public Health Service.

for the corresponding period. In the New England and East South Central sections the numbers of cases were approximately twice the number reported for the same weeks in 1947 and minor increases were reported from the North Central and Pacific sections. The current incidence in each section was, however, below the median for the five preceding years.

Poliomyelitis: The 111 cases of poliomyelitis reported for the four weeks ended February 28 was 60% of the number reported for the corresponding weeks in 1947 and 78% of the 1943-47 median. The Middle Atlantic, South Atlantic, and Mountain sections each reported a few more cases than might normally be expected, but in other sections the incidence was either the same as the median or fell below it. For the country as a whole the current incidence was the lowest since 1944 when 90 cases were reported for this same period.

Scarlet fever: This disease continued at an unprecedented low level, 9,626 cases being reported for the current four weeks as compared with 11,017 in 1947 and a median of 16,265 cases for the corresponding period in the preceding five years. The incidence was below the median in all sections of the country with the greatest declines occurring in the North Atlantic sections and the

smallest in the South Central sections. For the country as a whole the current incidence was the lowest for this period in the 20 years for which data are available in this form.

Smallpox: Fourteen cases of smallpox were reported for the four weeks ended February 28. During the same weeks in 1947 there were 13 cases reported and the median for the preceding five years was 43 cases. Four cases occurred in the East North Central section, five in the West South Central section, and the remaining five cases were widely distributed over the country.

Typhoid and paratyphoid fever: The number of cases (149) of these diseases was the lowest reported for these same weeks in the 20 years for which these data are available. In the East North Central section the incidence was 1.3 times the median for the five preceding years (1943-47), but in all other sections the incidence was below the seasonal expectancy.

Whooping cough: The incidence of whooping cough (8,556 cases) was about 83% of the 1947 incidence for the same period and 91% of the median for the five preceding years (9,357 cases). The greatest increase over the normal seasonal incidence was reported from the West South Central and Mountain sections and the greatest declines occurred in the North Atlantic sections.

Mortality, All Causes

For the four weeks ended February 28 there were 41,179 deaths from all causes reported to the National Office of Vital Statistics by 93 large cities. The median number for the corresponding period in the years 1945-47 was 39,599. The number of deaths was higher than the median for the three preceding years in the first three weeks of the current period, but during the last week of the period the number of deaths was 4% below the three-year median.

BOOK REVIEWS

Diseases of the Chest, with Emphasis on X-Ray Diagnosis, Eli H. Rubin, M.D., and Morris Rubin, M.D., $14.50, 685 pages, 760 illustrations with 24 plates in color. W. B. Saunders Co., Philadelphia 5 and London, 1947.

This book is particularly suited to general practitioners and the emphasis given to X-ray is well demonstrated throughout. It is primarily an application of the method of X-ray as a clinical instrument to aid the clinician.

The broad aspects of chest disease including anatomy and physiology are developed with a consideration of pathogenesis in various specific conditions. The pneumonias are considered from an etiologic standpoint which is very important if proper understanding and treatment is to be attained. Emphasis is given to the importance of history and the skill required to get a good history. The significance of a good physical examination is not minimized, and the help to be obtained from X-ray is obvious in the book.

There is little information on pneumonias or chest conditions of infancy but on the other hand, attention is given to pulmonary diseases of childhood. Therapy of acute bacterial pneumonias is dealt with in a separate chapter and includes the use of sulfa drugs, penicillin, and streptomycin with attention to the use of the latter in aersols. A small section is devoted to new immunization methods for pneumococcic pneumonias. A considerable portion of the book is given over to tuberculosis and all aspects of this important problem are considered in detail. A very interesting chapter on pulmonary diseases caused by higher bacteria and fungi will be found to be instructive and provocative of thought on the increasing importance of these diseases today. The principles of chest surgery and therapeutic possibilities are dealt with briefly in the last 50 pages with adequate illustrations for the non-surgical reader.

The bibliography throughout is separated into diseases and is most helpful when presented in this manner.

John M. Adams

The Rh Factor in the Clinic and the Laboratory. Special Issue No. 2 of Blood, The Journal of Hematology. Edited by Joseph M. Hill, M.D., and William Dameshek, M.D., $4.25, 192 pages. Grune and Stratton, New York 16, 1948.

In November, 1946, an International Hematology and Rh Conference was held in Dallas, Tex.-Mexico City. This volume records most of the papers and discussions presented at the conference on subjects pertaining to the Rh factor. Clinicians will be particularly interested in a paper by Chown on variations in erythroblastosis fetalis, a paper by Davidsohn on correlation of Rh antibodies with clinical findings, and a paper by Wallerstein on treatment of erythroblastosis fetalis by substitution transfusion. Other reports, such as those on the relationship of the A and B factors to the Rh factor and to erythroblastosis fetalis, and a paper on a possible third order of antibodies, suggest new fields of investigation and techniques of serologic diagnosis. The volume contains an excellent discussion by Race of the Rh genotypes and Fisher's theory of three gene loci; no defense of the Wiener theory of multiple alleles is presented. A discussion of hemolytic mechanisms by Dameshek is a valuable contribution. There are editorial shortcomings, such as the omission of a paper read at the Conference by Diamond on physicochemical and immunologic characteristics of Rh antibodies and the inclusion of other material which seems remotely related to Rh. The title suggests that this book is a general survey of the subject; however, it will prove of primary interest to research workers or others who are already familiar with the field.

Neva M. Abelson

Rh . . . Its Relation to Congenital Hemolytic Disease and to Intragroup Transfusion Reactions. Edith L. Potter, M.D., $5.50, 344 pages. The Year Book Publishers, Inc., Chicago 4, 1947.

Since discovery of the importance of the Rh antigen, more than 700 papers have appeared in the various fields of investigation which this discovery has opened. Many of these papers have been

controversial or trivial, and no satisfactory digest of the literature has been available. Therefore, the appearance of a comprehensive, authoritative review of present knowledge and theories concerning the Rh factor is singularly welcome. In this volume the author has included clear, impartial, and well-illustrated discussions of the genetics, nomenclature, and serologic detection of the Rh antigens and antibodies; the clinical and pathologic manifestations of hemolytic disease, and the relation of Rh to transfusion reactions. The division of hemolytic disease into five rather than the usual three groups seems awkward, and the exchange transfusion is discussed more briefly than its present popularity warrants. These, however, are minor objections, and this book can be recommended without reservation to clinicians and laboratory workers who are seeking clarification of an important but rapidly-changing and complicated subject.

NEVA M. ABELSON

BLOOD DERIVATIVES AND SUBSTITUTES, Charles Stanley White, M.D., and Jacob Joseph Weinstein, M.D., $7.50, 530 pages, 196 figures. The Williams & Wilkins Company, Baltimore 2, 1947.

Since the advent of blood banking in the United States in 1937 vast advances in the preparation, storage and utilization of blood, blood derivatives and substitutes have occurred. The second World War provided additional stimulus for the investigation of the potentialities of these substances. It is therefore appropriate for the authors of this volume to summarize the accumulated knowledge concerning blood derivatives and substitutes as they have long been active in investigations in this field.

The volume is well organized and comprehensive in its scope. From a concise historic discussion the authors proceed to consider the fundamental chemistry and physiology of plasma. The chapters on preparation, storage and administration are extremely practical while providing adequate theoretic background and should make this volume a convenient handbook for anyone concerned in any way with the handling of blood derivatives and substitutes. While the chapter on plasma fractionation and fractions presents recent trends quite well, one cannot help but note the omission of any discussion of antihemophilic globulin.

Plasma substitutes are effectively and concisely considered and many practical suggestions concerning administration of these substances are made. A comprehensive discussion of shock and its management is presented. The discussion of the clinical results with human plasma, while generally sound, occasionally reflects the authors' enthusiasm for their product rather than objective evaluation. Thus the claims made for the value of plasma in the management of the prematurely born infant do not appear too well substantiated by the data which the authors present.

The text is well written and the typography is excellent. The illustrations are clear, pertinent and adequate. The bibliographies at the conclusion of each chapter are well selected. This volume can be recommended to all concerned with either the theoretic or practical aspects of blood derivatives and substitutes.

HENRY G. PONCHER

COLOR ATLAS OF HEMATOLOGY, Roy R. Kracke, M.D., $5.00, 204 pages, 35 illustrations, part in color. J. B. Lippincott Co., Philadelphia 5, 1947.

There has always been a demand for a practical work book on hematology among students of medicine, practitioners and laboratory technicians that would provide a ready reference source when examining blood films. A number of such books have appeared in recent years and have been well received. Many of those which have been published are now out of date or incomplete in their coverage of the practical aspects of current advances in the field of hematology. This volume was prepared by Doctor Kracke utilizing the plates from his large treatise, "Diseases of the Blood" and incorporating concise clinical descriptions of various disorders of hematopoiesis together with other desirable hematologic findings that makes this a practical, concise and current working manual. The book contains 32 plates in full color of all the commonly known hematologic disorders and 3 plates in black and white. In general, these are not well done, lacking the fidelity that an atlas on hematology should provide. The immature cells illustrated lack the morphologic detail in nuclear structure that is so vital for the novice in differentiating one cell from another. The mature cells

on the other hand are well done. The organization of the altas is good and it is divided into 23 concise chapters. The first chapter deals with terminology of blood diseases and the second chapter presents the origin and development of the normal and abnormal cellular elements of the blood illustrated with a black and white plate and an inferior colored plate which leaves much to be desired in fidelity of color and cellular structure. The author represents the megaloblast as the precursor of the normal red cell series according to the view of Sabin and Doan. This is a debatable point and in the light of recent work is not consistent with clinical interpretations. The next chapters deal with a discussion of leucocytosis and leucopenic states, including causes, diagnosis and treatment; anemic states, their classification, etiology, clinical and laboratory findings and treatment, Anemias of Infancy and Childhood are inadequately presented in this chapter but are scattered throughout the various chapters in the book. The next chapters deal with the leukemic states, hemorrhagic diseases, and other diseases of the blood-forming organs. Acute Infectious Lymphocytosis is not discussed and should have been included. There are concise discussions of bone marrow, splenomegaly and splenectomy and blood parasites. The chapter on blood pictures in various laboratory animals is unique and valuable. Hematologic technic is concisely outlined and critically presented in an adequate manner. The last chapter deals with a summary of the hematologic findings in various diseases and a list of references is appended where the reader may expand the concise descriptions given by the author. The book will find its greatest value for men in general practice as a concise summary of hematology.

HENRY G. PONCHER

THE SPLEEN AND HYPERSPLENISM, William Dameshek, M.D., and Solomon Estren, M.D., $4.75. Grune and Stratton, Inc., New York 16, 1948.

Some years ago Doctor Dameshek and his group prepared a reprint of their exhibit on Hemolytic Syndromes presented at the 1942 Convention of the American Medical Association at Atlantic City. This work on The Spleen and Hypersplenism is a comparable publication consisting of a reprint of an exhibit presented at the 100th Anniversary Convention of the American Medical Association in June 1947. Publications of this type have answered an expressed desire on the part of physicians who have attended the scientific sessions of the Convention of the American Medical Association. The value of the work is that it correlates material in a broad field of medicine in a succinct form utilizing visual and mnemonic technics. Doctor Dameshek and his group are particularly fitted to present this subject as they have been continuously occupied with synthesizing data and clinical material in this field for years. The work is well illustrated with colored plates on the gross anatomy of the spleen, black and white illustrations of blood pictures, bone marrow smears and histologic sections of the spleen. Charts, diagrams and tabulated facts serve to fix salient points of presentation. Epitomized material on the anatomy, histology, and physiology of the spleen are presented together with a review of the pathologic physiology of hypersplenism. The role of the spleen in hemolytic anemias, idiopathic thrombocytopenic purpura, cytopenic and neutropenic states, is reviewed. The pathogenesis of hypersplenic syndromes and causes for splenomegaly are given in epitomized form and the diagnostic laboratory and clinical approach, together with pertinent facts on splenectomy are summarized. The publication is lithographed employing large-sized calligraphy in red and black colors for the written material and is put together with a ring binder. It is a unique type of publication and should serve a specialized function in one's library as monographic compendium with visual aids on the subject of the spleen and hypersplenism.

HENRY G. PONCHER

HISTORY OF NURSING, Gladys Sellew, Ph.D., R.N., and C. J. Nuesse, Ph.D., $3.75, 440 pages. The C. V. Mosby Co., St. Louis 3, 1946.

The keynote of the book is found in the preface where it is stated that "the central thesis of the authors is the inextricable interweaving of nursing service with all other branches of human culture." The development of nursing is traced through the record of human history starting with primitive times and ending with the problems facing the world at the conclusion of World War II.

Up to the middle of the 19th century, nursing was under the auspices of religious orders. After the Protestant revolt, nursing as a profession for lay people began to take root. Training was provided for young women and the religious orders, along with lay groups, opened their institutions

for the teaching of nursing. Many schools developed at a cost of poor training but of advantage to the hospitals which profited by the free labor of the students. Through the efforts of the members of the nursing group, standards were set, schools of nursing on a collegiate level were established and opportunities for professional growth were assured. The status of nursing in every part of the world is graphically described and the problems of the day confronting the professional nurses in our own country are clearly enumerated.

The text is intended primarily for students of nursing in Catholic institutions. The summary at the end of each chapter followed by suggested questions for study as well as a reading list on related topics make the book excellent for student teaching.

BORIE TOTH, R.N.

HISTOPATHOLOGY OF THE EAR, NOSE AND THROAT, Andrew A. Eggston, M.D., and Dorothy Wolff, M.A., Ph.D., $18.00. 1080 pages, 505 illustrations and 28 color plates. The Williams & Wilkins Co., Baltimore 2, 1947.

Until the appearance of this volume a study of the histopathology of the ear, nose and throat was largely a matter of searching the library for incidental paragraphs in textbooks and current journals. This first comprehensive volume on the subject is complete and authentic.

While the subject at large may not concern the pediatrician, he will find the description of otitis media, nasal infections and tonsillitis of special interest, as well as a chapter on oral and pharyngeal pathological manifestations of constitutional disease.

ARTHUR W. PROETZ

SCHOOL HEALTH PROBLEMS, by Laurence B. Chenoweth, M.D. and Theodore K. Selkirk, M.D. (With an Outline on School Health Administration by Richard Arthur Bolt, M.D., Dr. P. H.) Third Edition, $3.00, 419 pages, 116 figures. F. S. Crofts & Co., New York 3, 1947.

A text for students of education and teachers in service. Attempts to show what problems exist in the field of school health. No important changes have been made in this edition printed after seven years.

PEDIATRIC GYNECOLOGY, by Goodrich C. Schauffler, M.D., Second Edition, $6.00, 380 pages, 75 figures. The Year Book Publishers, Inc., Chicago 4, 1947.

A review* of the first edition of this book indicated that it was an outstanding contribution to pediatric literature. It still occupies a unique position, being the only one of its kind and also is presented in a form and with a philosophy which should be acceptable to pediatricians. It should be of service to any one concerned with children. While the subject may be somewhat restricted, it is one which frequently concerns the care of a child, chiefly the adolescent girl. More and more the pediatrician is concerned with this age level. Advances in endocrinology, for one thing, bring children to the doctor for direction and care not only in a strict gynecologic sense but also as a part of the extensive changes in the growth process at this age. The author has emphasized the value of the book from a medicolegal aspect, one which may be of concern occassionally to the pediatrician.

The new edition shows many minor changes throughout the text. These have been made in keeping with advances in the many aspects of the subject which are covered. The book remains, as was stated previously, an unusual source of information and value to the pediatrician as a specialist and as a consultant, and also to the general practicing physician. The author maintains still a conservative attitude in his approach to every phase of the subject.

PHARMACOLOGY THERAPEUTICS AND PRESCRIPTION WRITING. Walter Arthur Bastedo, M.D., Sc.D. (Hon.), Fifth Edition, $8.50, 840 pages, 82 figures, W. B. Saunders Company, Philadelphia 5, 1947.

---

* J. PEDIAT. 21:286, 1942.

Includes revision of the United States Pharmacopoeia, Edition XIII and The National Formulary, Edition VIII. The present edition has been rewritten after ten years. A useful reference.

DISEASES OF THE NOSE, THROAT AND EAR, by Howard Charles Ballenger, M.D., assisted by John Jacob Ballenger, M.D., Ninth Edition, $12.50, 993 pages with 597 illustrations and 16 plates in color. Lea & Febiger, Philadelphia 6, 1947.

For this Ninth Edition, the name of Dr. John Jacob Ballenger appears as a junior author. Considerable revision has been made in special chapters by Dr. J. D. Kelly in describing his technique of arytenoidectomy. Chapters by Dr. Alfred Lewy on "Physiology and Functional Tests of the Labyrinth" and "Inflammatory Diseases of the Labyrinth" and by Drs. Gabriel Tucker and C. L. Jackson on "Peroral Endoscopy" have been extensively revised. There is a great deal of information for reference by pediatricians in this book.

ROENTGEN INTERPRETATION, by George W. Holmes, M.D., and Laurence L. Robbins, M.D., Seventh Edition, $7.00, 398 pages with 266 illustrations. Lea & Febiger, Philadelphia 6, 1947.

Dr. Robbins, the junior author, has taken over from Dr. Ruggles for this new Seventh Edition. The principal changes which have been introduced are that the illustrations are now presented in positive instead of negative form. The change over isn't complete because many old forms were not available for re-illustration. The other changes consist of those related to new methods of diagnosis and treatment in which the roentgen ray plays a part.

NEWS AND ANNOUNCEMENTS

Post-graduate Education: A three day post-graduate course in Well Child Supervision will be given this April 26, 27, and 28 at the Medical Center in Denver. It is being sponsored by the Colorado State Department of Public Health, the Rocky Mountain Pediatric Society and the University of Colorado Medical Center.

It is intended primarily for the physicians of Colorado, but other physicians interested may apply for it by writing to the Director of Graduate and Post-Graduate Medical Education, University of Colorado Medical Center, 4200 East Ninth Avenue, Denver 7, Colorado. There is no registration fee.

* * *

Washington University School of Medicine, Division of Postgraduate Studies, St. Louis, announces a one-week course in Pediatrics, beginning May 24, 1948 at the St. Louis Children's Hospital. Further information as to subject matter may be obtained from the Director of the Division, 4580 Scott Avenue, St. Louis 10, Mo.

* * *

News of the death on January 31, 1948 of Dr. Albert H. Montgomery of Chicago, an Associate Fellow, has been received.

EDITORIAL

THE Original Article in this issue of Pediatrics by Byers and Moll on encephalopathies following prophylactic pertussis vaccine will be a cause of the gravest concern to all pediatricians. While the authors are reserved in expressing an opinion as to the mechanisms responsible for the sequelae of pertussis vaccination which they describe, it is a matter of the most urgent importance that these be sought and made the basis for practical changes and improvements designed to minimize dangers which now clearly emerge, curiously enough fifteen years or so after active immunization against pertussis began to be used on a large scale in this country. At the same time, it should be pointed out that incontrovertible evidence is now at hand of the effectiveness of pertussis vaccine in preventing a disease which in the first two years of life has a very high fatality rate.

While complete answers to the problems raised by the paper of Byers and Moll cannot be given at the present time, it is pertinent to consider possible causes for the reactions they report and lines along which precautionary measures might profitably be directed.

The following five categories appear to us to include the principal possibilities:

1. Constitutional peculiarities of the patients themselves.
2. Inadvertent intravenous injection of vaccine.
3. Antigen-antibody response to previous specific sensitization.
4. The presence of pyrogens in the bacterial bodies or in the water used in the preparation of the vaccine.
5. Damage to the cerebral vessels from toxins of H. pertussis. These may be considered in order:

1. The only point in favor of the constitutional factor is the very small proportion of severe reactions relative to the enormous total number of immunizing injections given. It should not be considered seriously unless positive evidence is forthcoming and until other possibilities have been exhausted.

2. The immediate reaction observed in 2 of the 15 cases suggests that the material may have entered through the veins, a possibility that must be kept in mind with all subcutaneous and intramuscular injections. In these two cases, embolism is a possibility and pertussis vaccine does at times show distinct clumping. The similarity of the reactions in the two immediate cases to those appearing later and presumably not due to intravenous injection suggests, however, that the mechanism was the same in all and that if embolism occurred it was not the sole responsible factor.

Nevertheless, it is the physician's responsibility to take such precautions as are feasible against intravenous injection.

3. Specific antigen-antibody reactions to pertussis antigen do not appear to explain adequately the observations of Byers and Moll. Six of them followed the first injection. It is difficult à priori to believe that these infants had been specifically sensitized in utero or in early infancy, and no direct evidence, such as active immunization of the mothers during pregnancy, is offered. Of the six, five occurred within the first eight hours after inoculation, while of the twelve reactions following second or later injections only four occurred within the first eight hours; these time relationships do not follow the pattern to be expected from specific sensitization.

4. The case reports are somewhat suggestive of pyrogen reaction. In all cases in

which the temperature is mentioned, fever was present and when the degree is stated it was high.

It would appear to be most important that manufacturers use every precaution against the introduction of pyrogens into vaccine. The routine administration of aspirin after injections may have value.

5. Since H. pertussis contains toxins known to produce vascular damage, it seems highly probable that these constituted an important and perhaps the major factor in the phenomena under discussion. Again, since the latter occur only exceptionally, it may be surmised that only under exceptional conditions are the toxins present in commercial vaccine in sufficient amounts to exert seriously harmful effects. Two such conditions are known. It is well established that freshly prepared pertussis vaccines are more toxic than those which have been aged in the refrigerator. In one clinic where aged vaccines have been used almost exclusively for a period of more than 12 years, only two cases of febrile convulsions have occurred, neither of them with residual neurologic sequelae. It is possible that "raw" vaccine released and administered too soon after manufacture may have been responsible for some of the encephalopathies reported by Byers and Moll. Second, it is known that freezing and thawing liberates toxin from the bacterial cell, and the possibility of freezing during transportation or in electric refrigerators must be considered.

The National Institute of Health in March 1947 proposed routine testing of pertussis vaccine for toxicity, but it does not appear as yet that this is mandatory nor actually carried out regularly by all manufacturers. The tests now available for toxicity are probably not wholly reliable nor adequate, and further investigation of the subject is urgently needed. It appears to us that the standards for manufacture and distribution of pertussis vaccine should be set up at the earliest possible moment, preferably by the National Institute of Health, and made the basis for regulations to be strictly enforced on a national scale. We trust that the American Academy of Pediatrics will do everything in its power to promote this most important development, and it is encouraging to find that Dr. John A. Toomey, now President of the Academy, has already shown an active interest in the problem.

HAROLD K. FABER AND JOHN J. MILLER, JR.